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L1            49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "GALLOWAY D"/AU OR "GALLOWAY
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                 OR "GALLOWAY DARRELL RAY"/AU)


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=> d ibib abs l1 1-49

L1   ANSWER 1 OF 49  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:473715  HCAPLUS
DOCUMENT NUMBER:          135:209571
TITLE:                    Protection against anthrax lethal toxin challenge by
                          genetic immunization with a plasmid encoding the
                          lethal factor protein
AUTHOR(S):                Price, Brian M.; Liner, Adriane L.; Park,, Sukjoon;
                          Leppla, Stephen H.; Mateczun, Alfred; Galloway,
                          Darrell R.
CORPORATE SOURCE:         Department of Microbiology, The Ohio State University,
                          Columbus, OH, 43017-1292, USA
SOURCE:                   Infect. Immun. (2001), 69(7), 4509-4515
                          CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER:                American Society for Microbiology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   The ability of genetic vaccination to protect against a lethal challenge
     of anthrax toxin was evaluated.  BALB/c mice were immunized via gene gun
     inoculation with eucaryotic expression vector plasmids encoding either a
     fragment of the protective antigen (PA) or a fragment of lethal factor
     (LF).  Plasmid pCLF4 contains the N-terminal region (amino acids [aa] 10
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to 254) of Bacillus anthracis LF cloned into the pCI expression plasmid. Plasmid pCPA contains a biol. active portion (aa 175 to 764) of B. anthracis PA cloned into the pCI expression vector. One-micrometer-diam. gold particles were coated with plasmid pCLF4 or pCPA or a 1:1 mixt. of both and injected into mice via gene gun (1 .mu.g of plasmid DNA/injection) three times at 2-wk intervals. Sera were collected and analyzed for antibody titer as well as antibody isotype. Significantly, titers of antibody to both PA and LF from mice immunized with the combination of pCPA and pCLF4 were four to five times greater than titers from mice immunized with either gene alone. Two weeks following the third and final plasmid DNA boost, all mice were challenged with 5.50% LDs of lethal toxin (PA plus LF) injected i.v. into the tail vein. All mice immunized with pCLF4, pCPA, or the combination of both survived the challenge, whereas all unimmunized mice did not survive. These results demonstrate that DNA-based immunization alone can provide protection against a lethal toxin challenge and that DNA immunization against the LF antigen alone provides complete protection.

REFERENCE COUNT: 35

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:472432 HCAPLUS

DOCUMENT NUMBER: 135:75730

TITLE: Methods for protecting against lethal infection with Bacillus anthracis

INVENTOR(S): **Galloway, Darrell R.**; Mateczun, Alfred J.

PATENT ASSIGNEE(S): The Ohio State University Research Foundation, USA

SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045639	A2	20010628	WO 2000-US34912	20001221

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-171459 P 19991222

AB Methods of inducing an immune response which protects a susceptible animal subject from lethal infection with Bacillus anthracis (B. anthracis) are provided. One method comprises administering an effective amt. of wild-type, or preferably a mutated form of, B. anthracis lethal factor (LF) or an immunogenic fragment thereof to the subject. A second method

comprises administering an effective amt. of a mutated LF protein or an immunogenic fragment of an LF protein and an effective amt. of the B. anthracis protective antigen (PA) or an immunogenic fragment of the PA protein to the subject. A third method comprises administering a polynucleotide or nucleic acid comprising a sequence encoding a mutated B. anthracis LF protein or an immunogenic fragment of an LF protein to the subject. A fourth method comprises administering a polynucleotide which comprises a coding sequence for a mutated LF protein or an immunogenic fragment of an LF protein and a polynucleotide which comprises a coding sequence for the B. anthracis PA protein or an immunogenic fragment thereof to the subject. The present invention also relates to a protein or peptide based-immunogenic compn. for prepg. a vaccine which is capable of prophylactically protecting a subject against lethal effects of infection with B. anthracis or exposure to a toxic agent which is produced by B. anthracis. The protein or peptide based immunogenic compn. comprises a purified or recombinant LF protein or immunogenic fragment thereof and a purified or recombinant PA protein or immunogenic fragment thereof. The present invention also relates to a nucleic acid-based immunogenic compn. comprising a nucleic acid which comprises a sequence encoding the LF protein or an immunogenic fragment thereof and a polynucleotide which comprises a sequence encoding the PA protein or an immunogenic fragment thereof.

L1 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:309967 HCAPLUS
DOCUMENT NUMBER: 135:75462
TITLE: Protection against Pseudomonas aeruginosa chronic lung infection in mice by genetic immunization against outer membrane protein F (OprF) of P. aeruginosa
AUTHOR(S): Price, Brian M.; **Galloway, Darrell R.**; Baker, Neil R.; Gilleland, Linda B.; Staczek, John; Gilleland, Harry E., Jr.
CORPORATE SOURCE: Department of Microbiology, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Infect. Immun. (2001), 69(5), 3510-3515
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Pseudomonas aeruginosa major constitutive outer membrane porin protein OprF, which has previously been shown to be a protective antigen, was targeted as a DNA vaccine candidate. The oprF gene was cloned into plasmid vector pVR1020, and the plasmid vaccine were delivered to mice by biolistic (gene gun) intradermal inoculation. Antibody titers in antisera from immunized mice were detd. by ELISA, and the elicited antibodies were shown to be specifically reactive to OprF by immunoblotting. The IgG (IgG) immune response was predominantly of the IgG1 isotype. Sera from DNA vaccine-immunized mice had significantly greater opsonic activity in opsonophagocytic assays than did sera from control mice. Following the initial immunization and two consecutive boosts, each at 2-wk intervals, protection was demonstrated in a mouse model of chronic pulmonary infection by P. aeruginosa. Eight days post-challenge, both lungs were removed and examd. A significant redn. in the presence of severe macroscopic lesions, as well as in the no. of bacteria present in the lungs, was seen. Based on these findings, genetic immunization with oprF has potential for development as a vaccine to protect humans against infection by P. aeruginosa.
REFERENCE COUNT: 55
REFERENCE(S): (2) Allsopp, C; Eur J Immunol 1996, V26, P1951 HCAPLUS

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:852942 HCAPLUS
DOCUMENT NUMBER: 134:209635
TITLE: n-Butane isomerization on sulfated zirconia: active site heterogeneity and deactivation
AUTHOR(S): Kim, S. Y.; Goodwin, J. G.; **Galloway, D.**
CORPORATE SOURCE: Department of Chemical and Petroleum Engineering, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Catal. Today (2000), 63(1), 21-32
CODEN: CATTEA; ISSN: 0920-5861
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fast deactivation of sulfated zirconia (SZ) has limited its use in com. processes such as n-butane isomerization. In order to investigate this deactivation, steady-state isotopic transient kinetic anal. (SSITKA) was utilized to study in situ changes in surface kinetic parameters for n-butane isomerization on a widely studied SZ at 150.degree.C. Approx. 20% of the sulfate species was found to be n-butane adsorption sites, but only 1-2% of the sulfate species appeared to adsorb active surface reaction intermediates. The decrease in catalytic activity during deactivation could be attributed to the loss of active sites. The change in TOFITK* (TOF based on an av. residence time of active surface intermediates) and the regeneration characteristics of the SZ catalyst suggest a possible active site heterogeneity. It appears that the high initial activity and the fast deactivation for TOS.ltoreq.100 min were mainly due to the presence and deactivation of the more active sites, resp. Following the loss of the more active sites, the less active sites provided the majority of the catalytic activity obsd. for TOS.gtoreq.100 min. The less active sites appeared to be more easily regenerated than the more active sites as the catalytic activity at TOS.gtoreq.100 min was recovered following regeneration at 315.degree.C. Loss of active sites due to sulfur loss or migration seems unlikely. Site blockage by coke/oligomer formation appeared to be a significant contributor for catalyst deactivation for n-butane isomerization on SZ. The impact of sulfur redn. on catalyst deactivation cannot be ruled out at this point.
REFERENCE COUNT: 56
REFERENCE(S): (1) Adeeva, V; J Catal 1995, V151, P364 HCAPLUS
(2) Alvarez, W; Appl Catal A 1997, V162, P103 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:676395 HCAPLUS
DOCUMENT NUMBER: 133:361713
TITLE: Pseudomonas Exotoxin-Mediated Delivery of Exogenous Antigens to MHC Class I and Class II Processing Pathways
AUTHOR(S): Lippolis, John D.; Denis-Mize, Kimberly S.;

Brinckerhoff, Laurence H.; Slingluff, Craig L., Jr.; **Galloway, Darrell R.**; Engelhard, Victor H.
CORPORATE SOURCE: Department of Microbiology, University of Virginia, Health Sciences Center, Charlottesville, VA, 22908, USA
SOURCE: Cell. Immunol. (2000), 203(2), 75-83
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptides assocd. with class II MHC mols. are normally derived from exogenous proteins, whereas class I MHC mols. normally assoc. with peptides from endogenous proteins. We have studied the ability of Pseudomonas exotoxin A (PE) fusion proteins to deliver exogenously added antigen for presentation by both MHC class I and class II mols. A MHC class II-restricted antigen was fused to PE; this mol. was processed in a manner typical for class II-assocd. antigens. However, a MHC class I-restricted peptide fused to PE was processed by a mechanism independent of proteasomes. Furthermore, we also found that the PE fusion protein was much more stable in normal human plasma than the corresponding synthetic peptide. We believe that effective delivery of an antigen to both the MHC class I and class II pathways, in addn. to the increased resistance to proteolysis in plasma, will be important for immunization. (c) 2000 Academic Press.
REFERENCE COUNT: 39
REFERENCE(S):
(1) Allured, V; Proc Natl Acad Sci USA 1986, V83, P1320 HCAPLUS
(2) Armstrong, T; Proc Natl Acad Sci USA 1997, V94, P6886 HCAPLUS
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(4) Brinckerhoff, L; Int J Cancer 1999, V83, P326 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:50289 HCAPLUS
DOCUMENT NUMBER: 132:206667
TITLE: Analysis of immunization with DNA encoding Pseudomonas aeruginosa exotoxin A
AUTHOR(S): Denis-Mize, K. S.; Price, B. M.; Baker, N. R.; **Galloway, D. R.**
CORPORATE SOURCE: Department of Microbiology, The Ohio State University, Columbus, OH, USA
SOURCE: FEMS Immunol. Med. Microbiol. (2000), 27(2), 147-154
CODEN: FIMIEV; ISSN: 0928-8244
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The promising arena of DNA-based vaccines has led us to investigate possible candidates for immunization against bacterial pathogens. One such target is the opportunistic pathogen Pseudomonas aeruginosa which produces exotoxin A (PE), a well-characterized virulence factor encoded by the toxA gene. In its native protein form, PE is highly cytotoxic for susceptible eukaryotic cells through ADP-ribosylation of elongation factor-2 following internalization and processing of the toxin. To study the biol. and immunol. effects of PE following in situ expression, we have constructed eukaryotic plasmid expression vectors contg. either the

wild-type or a mutated, non-cytotoxic toxA gene. In vitro anal. by transfection of UM449 cells suggests that expression of the wild-type toxA gene is lethal for transfected cells whereas transfection with a mutated toxA gene results in the prodn. of inactive PE which can be readily detected by immunoblot anal. of cell lysates. To investigate the effects resulting from the intracellular expression of potentially cytotoxic gene products in DNA vaccine constructs, we immunized mice with both the wild-type and mutant toxA plasmid constructs and analyzed the resulting humoral and cellular immune responses. Immunization with the mutated toxA gene results in prodn. of neutralizing antibodies against native PE and potentiates a TH1-type response, whereas only a minimal humoral response can be detected in mice immunized with wild-type toxA. DNA-based vaccination with the non-cytotoxic toxAmut gene confers complete protection against challenge with the wild-type PE. Therefore, genetic immunization with genes encoding potentially cytotoxic gene products raises concern with regard to the selection of feasible gene targets for DNA vaccine development.

REFERENCE COUNT: 32

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:589745 HCAPLUS
DOCUMENT NUMBER: 129:299508
TITLE: Pseudomonas aeruginosa LasD processes the inactive LasA precursor to the active protease form
AUTHOR(S): Park, SukJoon; **Galloway, Darrell R.**
CORPORATE SOURCE: Department of Microbiology, Ohio State University, Columbus, OH, 43210-1292, USA
SOURCE: Arch. Biochem. Biophys. (1998), 357(1), 8-12
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB LasA and LasD are staphylolytic proteinases which are secreted by the opportunistic pathogen Pseudomonas aeruginosa. We have previously described the purifn. and characterization of both LasA and LasD, a 21-kDa protein which shares many of the enzymic properties of LasA. In this follow-up study we describe the isolation of the 42-kDa precursor of LasA (pro-LasA) and demonstrate the ability of the purified LasD proteinase to cleave the inactive proLasA to the 20-kDa active form of the proteinase. (c) 1998 Academic Press.

L1 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:419523 HCAPLUS
DOCUMENT NUMBER: 129:188082
TITLE: Development and analysis of exotoxin A fusion proteins for the exogenous delivery of peptide antigens
AUTHOR(S): **Galloway, D. R.**; Denis-Mize, K. S.; Lippolis, J. D.; Engelhard, V. H.; Brinckerhoff, L. H.; Slingluff, C. L., Jr.
CORPORATE SOURCE: Department of Microbiology, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Zentralbl. Bakteriol., Suppl. (1997), 29(Bacterial

Protein Toxins), 466-467
CODEN: ZBASE2; ISSN: 0941-018X
PUBLISHER: Gustav Fischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two model systems, representing both CD4+ and CD8+ T cell responses, have been employed to examine the efficacy of recombinant, non-cytotoxic Pseudomonas aeruginosa exotoxin A (PEI-II) for peptide delivery to either MHC class I or MHC class II processing pathways. The MHC class I model utilizes human cytotoxic T lymphocytes (CTLs) which recognize a melanoma-specific peptide (MEL-946). Using PEI-II with the MEL-946 fused in frame at the C-terminus (PE-946), the authors have demonstrated exogenous delivery of the nine residue melanoma-specific peptide to MHC class I mols. Chromium release assays for CTL activity confirmed that the that the PEI-II-MEL946 chimera stimulates an HLA A.2-restricted CTL response. A second model system was used to illustrate PEI-II-mediated delivery of peptides to MHC class II mols., using recombinant PEI-II protein linked to the proinsulin polypeptide (PEI-II-PI). The addn. of exogenous PEI-II-PI to antigen-presenting cells and insulin-specific murine CD4+ T cell clones results in IL-2 prodn. in vitro, indicative of T cell recognition of insulin epitopes in the context of MHC class II mols.

L1 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:589692 HCAPLUS
DOCUMENT NUMBER: 123:50653
TITLE: Purification and characterization of LasD: a second staphylolytic proteinase produced by Pseudomonas aeruginosa
AUTHOR(S): Park, Sukjoon; **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiology, Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: Mol. Microbiol. (1995), 16(2), 263-70
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors previously described studies of a 22-kDa active fragment of the LasA proteinase. In follow-up studies of LasA, the authors discovered the sep. existence of a 23-kDa proteinase which shares many of the enzymic properties of LasA, including the ability to lyse heat-killed staphylococci. However, this apparent serine proteinase, which was designated LasD, was distinct from the 22-kDa active LasA protein for the following reasons: (1) the N-terminal sequence of LasD shared no homol. with LasA or the LasA precursor sequence; (2) Pseudomonas aeruginosa LasA mutant strains AD1825 and FRD2128 did not produce LasA yet produced LasD; and (3) specific antibodies to each proteinase did not show any cross-reactivity. LasD appeared to be produced as a 30-kDa protein, which is possibly cleaved to produce a 23-kDa active fragment. The purified LasD fragment (23 kDa) showed strong staphylolytic activity only at higher pH conditions, whereas LasA exhibited staphylolytic activity over a broad pH range. In addn. to their ability to cleave at internal diglycine sites, both the LasD and LasA proteinases efficiently cleaved .beta.-casein.

L1 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:558739 HCAPLUS
DOCUMENT NUMBER: 123:7917
TITLE: Construction and use of a nontoxigenic strain of Pseudomonas aeruginosa for the production of recombinant exotoxin A

AUTHOR(S): Wozniak, Daniel J.; Han, Xiang Y.; **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiology, Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Appl. Environ. Microbiol. (1995), 61(5), 1739-44
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To express recombinant forms of Pseudomonas aeruginosa exotoxin A in high yield, the authors have developed a nontoxigenic strain of P. aeruginosa derived from the hypertoxigenic strain PA103. The nontoxigenic strain, designated PA103A, was produced by the excision marker rescue technique to replace the toxA structural gene in PA103 with an insertionally inactivated toxA gene. The PA103A strain (ToxA-) was used subsequently as the host strain for the expression and prodn. of several recombinant versions of exotoxin A, and the results were compared with exotoxin A prodn. in other P. aeruginosa and Escherichia coli strains. Use of the PA10dA strain transformed with the high-copy-no. pRO1614 plasmid bearing various toxA alleles resulted in final purifn. yields of exotoxin A averaging 23 mg/L of culture. By comparison, exotoxin A prodn. in other expression systems and host strains yields approx. 1/4 to 1/10 as much toxin.

L1 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:398189 HCAPLUS
DOCUMENT NUMBER: 123:2555
TITLE: ToxR (RegA) activates Escherichia coli RNA polymerase to initiate transcription of Pseudomonas aeruginosa toxA
AUTHOR(S): Walker, S. L.; Hiremath, L. S.; **Galloway, D. R.**
CORPORATE SOURCE: Department of Microbiology, The Ohio State University, Columbus, OH, 43210-1292, USA
SOURCE: Gene (1995), 154(1), 15-21
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Pseudomonas aeruginosa (Pa) structural gene (toxA), which encodes the exotoxin A protein has been shown to be regulated at the transcriptional level by a protein designated ToxR (also known as RegA). It was previously reported that ToxR directly enhances toxA transcription in vitro; however, in the absence of ToxR, Pa RNA polymerase (RNAP) transcribes toxA with low efficiency. The present study examd. the ability of ToxR to initiate toxA transcription using the heterologous Escherichia coli (Ec) RNAP and found that ToxR can function with Ec RNAP to efficiently transcribe toxA both in vitro and in vivo. Antibodies produced against the .sigma.70 subunit of Ec RNAP inhibit ToxR-mediated enhancement of toxA transcription, suggesting that the RNAP holoenzyme (E.sigma.70) is required for transcriptional activation of toxA. Further, ToxR is required for open-complex formation at the toxA promoter. By selectively deleting toxA upstream sequences, a 214-bp region was localized contg. both the toxA promoter and a putative ToxR-binding site sufficient for ToxR-mediated transcription of toxA.

L1 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:316780 HCAPLUS
DOCUMENT NUMBER: 122:74345
TITLE: Active site mutations of Pseudomonas aeruginosa exotoxin A. Analysis of the His440 residue

AUTHOR(S): Han, Xiang Y.; **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: J. Biol. Chem. (1995), 270(2), 679-84
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pseudomonas aeruginosa exotoxin A (ETA) is a member of the family of bacterial ADP-ribosylating toxins which use NAD+ as the ADP-ribose donor. By analogy to diphtheria and pertussis toxins, the His440 residue ETA has been proposed to be one of the crit. residues within the active site of the toxin. In this study the role of this His440 residue was explored through site-directed mutagenesis which resulted in the prodn. of ETA proteins contg. Ala, Asn, and Phe substitutions at the 440 position. The His440-substituted ETA proteins were purified and analyzed. All substitutions at the 440 site displayed severely reduced ADP-ribosylation activity (>1000-fold). However, NAD glycohydrolase activity remained intact and in the case of ETAH440N actually increased 10-fold. NAD+ binding is not affected by substitutions at the 440 site as indicated by similar Km values for the ETA variants tested. Conformational integrity of the mutant toxins appears to be largely unaffected as assessed by anal. with a conformation-sensitive monoclonal antibody as well as sensitivity to proteinase digestion. In view of the location of His440 residue within or close to the proposed NAD+-binding site, these results suggest that His440 may be a catalytic residue involved in the transfer of the ADP-ribose moiety to the EF-2 substrate.

L1 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:286674 HCAPLUS
DOCUMENT NUMBER: 122:98688
TITLE: ToxR (RegA)-mediated in vitro transcription of Pseudomonas aeruginosa toxA
AUTHOR(S): Walker, S. L.; Hiremath, L. S.; Wozniak, D. J.; **Galloway, D. R.**
CORPORATE SOURCE: Department of Microbiology, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Gene (1994), 150(1), 87-92
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Exotoxin A (ETA) has been described as a major virulence factor produced by the opportunistic pathogen Pseudomonas aeruginosa. The transcription of the ETA structural gene (toxA) has been shown to be pos. regulated by the product of the toxR gene (also called regA). However, the mechanism by which ToxR regulates toxA transcription is still under investigation. We have expressed toxR in Escherichia coli under the control of the T7 promoter and purified the wild-type ToxR protein. We have also produced ToxR as a fusion protein consisting of the first 12 amino acids of the T7 capsid protein attached to the N terminus of the intact ToxR protein. In the present study we have developed and used an in vitro transcription assay in order to investigate the mechanism of ToxR-mediated transcriptional regulation of toxA. Under the conditions of this in vitro assay toxA transcription requires the toxR product in addn. to P. aeruginosa RNA polymerase (RNAP). Both the native and the T7::ToxR fusion proteins facilitate initiation of toxA transcription in vitro in the presence of Pseudomonas RNAP. Addnl. studies using (i) specific ELISA; (ii) indirect immunopptn.; and (iii) gel-filtration chromatog., indicate that ToxR binds to the purified Pseudomonas RNAP and strengthens the possibility that ToxR may be an alternative sigma factor. Furthermore,

the ToxR-mediated transcription of toxA is increased approx. threefold in the presence of crude cytoplasmic exts. from P. aeruginosa ToxR+ or ToxR-RegB- strains, indicating that addnl. factors play a role in the efficient and optimal transcription of toxA.

L1 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:599191 HCAPLUS
DOCUMENT NUMBER: 119:199191
TITLE: Regulation of toxin A synthesis in Pseudomonas aeruginosa
AUTHOR(S): Shumard, Christine M.; Wozniak, Daniel J.; **Galloway, Darrell R.**
CORPORATE SOURCE: Diagn. Div., Abbott Lab., Abbott Park, IL, 60064, USA
SOURCE: Pseudomonas aeruginosa Opportunistic Pathog. (1993), 59-77. Editor(s): Campa, Mario; Bendinelli, Mauro; Friedman, Herman. Plenum: New York, N. Y. CODEN: 59EYAG
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 70 refs. The role of toxin A (ETA) in virulence has provided the stimulus for investigations into the mechanism of its prodn. Regulation of ETA synthesis is a complex process involving many environmental as well as genetic factors, of which only a few have been defined precisely. The authors begin with a discussion of environmental influences on ETA synthesis. This is followed by a summary of current knowledge concerning the regulation of ETA expression at the mol. level. Finally, the authors discuss the relationship between the environmental and genetic factors that regulate ETA synthesis.

L1 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:578424 HCAPLUS
DOCUMENT NUMBER: 119:178424
TITLE: Role of exotoxins in the pathogenesis of P. aeruginosa infections
AUTHOR(S): **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: Pseudomonas aeruginosa Opportunistic Pathog. (1993), 107-27. Editor(s): Campa, Mario; Bendinelli, Mauro; Friedman, Herman. Plenum: New York, N. Y. CODEN: 59EYAG
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 132 refs. Topics discussed include the roles of exotoxin A, exoenzyme S, elastase, and phospholipases in Pseudomonas aeruginosa infection.

L1 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:526176 HCAPLUS
DOCUMENT NUMBER: 117:126176
TITLE: Pseudomonas aeruginosa exotoxin A interaction with eukaryotic elongation factor 2. Role of the His426 residue
AUTHOR(S): Kessler, Sean P.; **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: J. Biol. Chem. (1992), 267(27), 19107-11 CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal

LANGUAGE: English

AB P. aeruginosa exotoxin A (ETA) catalyzes the transfer of the ADP-ribose moiety of NAD+ onto eukaryotic elongation factor 2 (EF-2). To study the ETA site of interaction with EF-2, an immobilized EF-2 binding assay was developed. This assay demonstrates that ETA, in the presence of NAD+, binds to immobilized EF-2. Addnl., diphtheria toxin was also found to bind to the immobilized EF-2 in the presence of NAD+. Comparative anal. was performed with a mutated form of ETA (CRM 66) in which a histidine residue at position 426 has been replaced with a tyrosine residue. This immunol. cross-reactive, ADP-ribosyltransferase(ADPRT)-deficient toxin does not bind to immobilized EF-2, thus explaining its lack of ADPRT activity. ETA bound to immobilized EF-2 cannot bind the monoclonal antibody TC-1 which specifically recognizes the ETA epitope contg. His426. Immunopptn. of native ETA by mAb TC-1 is only achieved by incubating ETA in the presence of NAD+. Di-Et pyrocarbonate modification of the His426 residue blocks ETA binding to EF-2 and prevents the binding of the TC-1 antibody. Analogs of NAD+ contg. a reduced nicotinamide ring or modified adenine moieties cannot substitute for NAD+ in the immobilized binding assay. Collectively, these data support the proposal that the site of ETA interaction with EF-2 includes His426 and that a mol. of NAD+ is required for stable interaction.

L1 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:442375 HCAPLUS

DOCUMENT NUMBER: 117:42375

TITLE: Pseudomonas aeruginosa exotoxin A: immunochemical analysis of the catalytic domain reveals ADPRT toxin crossreactive epitope

AUTHOR(S): **Galloway, D. R.**; McGowan, J. L.; Anderson, D. C.

CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA

SOURCE: Zentralbl. Bakteriol., Suppl. (1992), 23(Bact. Protein Toxins), 231-3
CODEN: ZBASE2

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A combined approach using monoclonal antibodies and synthetic peptides has revealed the existence of a crossreactive epitope within the catalytic domain (domain III) P. aeruginosa exotoxin A (ETA). Several monoclonal antibodies prepd. against intact ETA have been shown to bind to ADP-ribosyltransferase toxins (ADPRT toxins) including diphtheria, cholera and pertussis toxin. The epitope for one of these mAbs (designated T20) has been localized to the major helical segment in domain III (the A helix) defined by ETA residues 419-432 (VERLLQAHRQLEER), and preliminary results suggest that T20 binds to residues in the sequence RQLEER. The authors investigations reveal that T20 inhibits the ADPRT of ETA, yet does not inhibit the binding of the NAD+ substrate, since NAD-glycohydrolase activity is not inhibited in the presence of antibody. This suggests that T20 blocks the access of EF-2 protein substrate to ETA, thus preventing the covalent modification of EF-2 by the ADPRT reaction. A systematic screening of overlapping synthetic peptides spanning the entire ETA sequence indicates that T20 binds to the 419-432 sequence. Antipeptide antisera to the ETA 419-432 and 427-438 sequences also crossreact with diphtheria, cholera and pertussis toxins, in addn. to ETA and homologous peptide. Furthermore, ETA peptides 419-432 and 427-438 block the binding of anti-DT antibody to DT. Significantly, these antipeptide antibodies markedly inhibit the ADPRT activity of both ETA and DT, yet do not inhibit the binding of NAD+. Recent work indicates that peptides based upon a

homologous sequence from pertussis toxin inhibit the binding of antisera to the ETA-based peptide sequences indicated above. Collectively, these results indicate the existence of a homologous site among ADPRT toxins and in the case of ETA and DT this site is assocd. with a functional activity which can be inhibited with site-specific antibody.

L1 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:422341 HCAPLUS
DOCUMENT NUMBER: 117:22341
TITLE: Further studies on Pseudomonas aeruginosa LasA: analysis of specificity
AUTHOR(S): Peters, J. E.; Park, S. J.; Darzins, A.; Freck, L. C.; Saulnier, J. M.; Wallach, J. M.; **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: Mol. Microbiol. (1992), 6(9), 1155-62
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Full elastolytic activity in P. aeruginosa is a result of the combined activities of elastase, alk. proteinase, and the lasA gene product, LasA. The results of this study demonstrate that an active fragment of the LasA protein which is isolated from the culture supernatant fraction is capable of degrading elastin in the absence of elastase, thus showing that LasA is a 2nd elastase produced by this organism. In addn., it is shown that LasA-mediated enhancement of elastolysis results from the sep. activities of LasA and elastase upon elastin. The LasA protein does not affect the secretion or activation of a proelastase as previously proposed in other studies. Furthermore, LasA has specific proteolytic capability, as demonstrated by its ability to cleave .beta.-casein. Preliminary anal. of .beta.-casein cleavage in the presence of various protease inhibitors suggests that LasA may be classified as a modified serine protease.

L1 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:674022 HCAPLUS
DOCUMENT NUMBER: 115:274022
TITLE: Pseudomonas aeruginosa elastase and elastolysis revisited: recent developments
AUTHOR(S): **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: Mol. Microbiol. (1991), 5(10), 2315-21
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with numerous refs.. With the detn. of the 3-dimensional structure of elastase and the probable identification of the active site and key residues involved in proteolytic activity, knowledge of the mol. details of this interesting protease is rapidly increasing. Pseudomonas elastase appears to be remarkably similar to the Bacillus metalloproteinase thermolysin. A further significant development has been the discovery of the lasA gene and the fact that Pseudomonas elastase and alk. proteinase appear to act in concert with the LasA protein to display the notable elastolytic activity exhibited by isolates of this organism. Biochem. and genetic studies indicate that LasA is a second elastase which may be an important virulence factor that has been overlooked in previous studies.

L1 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:671805 HCAPLUS
DOCUMENT NUMBER: 115:271805
TITLE: Pseudomonas aeruginosa LasB mutant constructed by insertional mutagenesis reveals elastolytic activity due to alkaline proteinase and the LasA fragment
AUTHOR(S): Wolz, C.; Hellstern, E.; Haug, M.; **Galloway, D. R.**; Vasil, M. L.; Doering, G.
CORPORATE SOURCE: Hyg.-Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Mol. Microbiol. (1991), 5(9), 2125-31
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extracellularly secreted endopeptidase elastase (LasB) is regarded as an important virulence factor of P. aeruginosa. It has also been implicated in the processing of LasA which enhances elastolytic activity of LasB. To investigate the role of LasB in virulence and LasA processing, a LasB-neg. mutant, PAO1E, was constructed by insertional mutagenesis of the LasB structural gene, lasB, in P. aeruginosa PAO. An internal 636 pb lasB fragment of the plasmid pRB1803 was ligated into a deriv. of the mobilization vector pSUP201-1. The resulting plasmid, pBRMOB-LasB, was transformed into Escherichia coli and transferred by filter matings to the LasB-pos. P. aeruginosa strain, PAO1. Plasmid integration in the lasB site of the chromosome was confirmed by Southern blot anal. RIA and immunoblotting of PAO1E supernatant fluids yielded no detectable LasB (<1 ng mL-1 LasB). The absence of LasB in PAO1E was further proven by the inability of its culture supernatant fluid to cleave transferrin or rabbit IgG (IgG) after 72 h incubation. The residual proteolytic activity of PAO1E culture supernatant fluid was attributed to alk. proteinase (Apr), since it was totally inhibited by specific antibodies against Apr. Residual elastolytic activity in culture supernatant fluid of PAO1E was due to the LasA fragment and to the combined action of the LasA fragment with Apr on elastin. The sizes of purified LasA from PAO1 and PAO1E were identical (22 kDa). These results show that, besides LasB and LasA fragment, Apr may also act on elastin in the presence of the LasA fragment and that the proteolytic processing of LasA in P. aeruginosa is independent of LasB.

L1 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:180070 HCAPLUS
DOCUMENT NUMBER: 114:180070
TITLE: Immunochemical analysis of Pseudomonas aeruginosa exotoxin A. Analysis of the His426 determinant
AUTHOR(S): McGowan, Jean L.; Kessler, Sean P.; Anderson, David C.; **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: J. Biol. Chem. (1991), 266(8), 4911-16
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study describes a combined immunochem. and genetic approach defining a site on P. aeruginosa exotoxin A (ETA) which is crit. to the ADP-ribosyltransferase (ADPRT) activity of the toxin. The sequential epitope of a monoclonal antibody (TC-1) which binds to domain III (residues 405-613), contg. the ADPRT activity of ETA, has been defined using a series of synthetic peptides. This epitope spans residues 422-432 which composes the major .alpha.-helical segment of domain III and includes His426 which has previously been shown to be essential for ADPRT

activity. The crit. His426 residue which projects into a major cleft becomes exposed when the ETA protein is in an ADPRT-active configuration. Since the TC-1 mAb does not block the binding of NAD+, it is possible that the .alpha.-helix site contg. the TC-1 epitope and the His426 residue is assocd. with the interaction between ETA and its elongation factor 2 substrate.

L1 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:36764 HCAPLUS
DOCUMENT NUMBER: 114:36764
TITLE: Revised nucleotide sequence of the lasA gene from Pseudomonas aeruginosa PAO1
AUTHOR(S): Darzins, A.; Peters, J. E.; **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Nucleic Acids Res. (1990), 18(21), 6444
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A comparison of the purified LasA active fragment with the published sequence of lasA revealed a significant inconsistency with the predicted size and isoelec. point (pI) of the active fragment. To address this discrepancy, a 1.7 kb SmaI-HindIII DNA fragment harboring the entire lasA gene was cloned from the P. aeruginosa PAO1 chromosome using an oligonucleotide probe and its nucleotide sequence was detd. by the dideoxy chain termination method. Juxtaposition of these sequences revealed differences in 10 nucleotide bp. The most significant change is the absence of a translation termination codon at position 1276 which increases the lasA reading frame by an addnl. 41 amino acids. Immediately following the new termination codon at position 1399 is a 40 bp region contg. a possible transcription termination signal. This revised sequence predicts an active LasA fragment size of 20 kDa which closely approximates the SDS-PAGE estd. wt. of 21 kDa. In addn., the predicted pI shifts from 7.48 to 9.24, a value which also corresponds closely with the pI of the purified active fragment. Since expression of the lasA gene in Escherichia coli results in the prodn. of a 40 kDa polypeptide, a new putative translational start to accommodate these changes is at position 289 (TTG) along with a Shine-Dalgarno (SD) sequence located about 12 bp upstream.

L1 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:626699 HCAPLUS
DOCUMENT NUMBER: 113:226699
TITLE: Purification of the pyocin S2 complex from Pseudomonas aeruginosa PAO1: analysis of DNase activity
AUTHOR(S): Seo, Younghoon; **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: Biochem. Biophys. Res. Commun. (1990), 172(2), 455-61
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pyocin S2 purified from mitomycin C-induced lysates of P. aeruginosa strain PAO1 has been to consist of a complex of 2 proteins. Further anal. of the purified S2 complex revealed that the 74-kd S2 pyocin demonstrates DNase activity which can be blocked by S2-specific antisera. Chromosomal DNA from pyocin cells treated with the pyocin S2 complex did not show any degrdn., suggesting that the 10-kd protein inhibits the DNase activity of the S2 protein. These results and alternative mechanism for the toxicity

assocd. with the S2 pyocin.

L1 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:419994 HCAPLUS
DOCUMENT NUMBER: 113:19994
TITLE: Purification and characterization of an active fragment of the LasA protein from Pseudomonas aeruginosa: enhancement of elastase activity
AUTHOR(S): Peters, John E.; **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: J. Bacteriol. (1990), 172(5), 2236-40
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A 22-kilodalton protein purified from the culture supernatant fraction of P. aeruginosa (strains PA220 and PAO1) was found to enhance the elastolytic activity of purified P. aeruginosa elastase. N-terminal sequence anal. identified the protein as a fragment of the lasA gene product. However, comparative anal. with the reported LasA sequence indicated that the purified LasA fragment was longer than the deduced sequence reported. The purified LasA fragment had minimal elastolytic and proteolytic activity and did not enhance the proteolytic activity of purified elastase, yet enhanced the elastolytic activity >25-fold. The LasA fragment was found to also enhance the elastolytic activities of thermolysin, human neutrophil elastase, and proteinase K. The results presented here suggest that the LasA protein interacts with the elastin substrate rather than modifying elastase.

L1 ANSWER 25 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:548527 HCAPLUS
DOCUMENT NUMBER: 111:148527
TITLE: Biochemical analysis of CRM 66. A nonfunctional Pseudomonas aeruginosa exotoxin A
AUTHOR(S): **Galloway, Darrell R.**; Hedstrom, Richard C.; McGowan, Jean L.; Kessler, Sean P.; Wozniak, Daniel J.
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210-1292, USA
SOURCE: J. Biol. Chem. (1989), 264(25), 14869-73
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A direct biochem. comparison was made between P. aeruginosa exotoxin A (ETA) and a nonenzymically active mutant toxin (CRM 66) using highly purified prepns. of each protein. The loss of ADP-ribosyltransferase activity and subsequent cytotoxicity were correlated with the presence of a tyrosine residue in place of a histidine at position 426 in CRM 66. In the native conformation, CRM 66 demonstrated a limited ability (by a factor or at least 100,000) to modify elongation factor 2 (EF-2) covalently and lacked in vitro and in vivo cytotoxicity, yet CRM 66 appeared to be normal with respect to NAD+ binding. Upon activation with urea and dithiothreitol, CRM 66 lost ADP-ribosyltransferase activity entirely yet CRM 66 retained the ability to bind NAD+. Replacement of Tyr-426 with histidine in CRM 66 completely restored cytotoxicity and ADP-ribosyltransferase activity. These results support previous findings from this lab. (1988) which suggest that the His-426 residue of ETA is not involved in NAD+ binding but appears to be assocd. with the interaction between ETA and EF-2.

L1 ANSWER 26 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:451313 HCAPLUS
DOCUMENT NUMBER: 111:51313
TITLE: Nucleotide sequence and characterization of toxR: a gene involved in exotoxin A regulation of Pseudomonas aeruginosa [Erratum to document cited in CA107(1):1681n]
AUTHOR(S): Wozniak, D. J.; Cram, D. C.; Daniels, C. J.; **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Nucleic Acids Res. (1989), 17(8), 3334
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An error in the original sequence in Figure 5 has been cor. The reading frame now becomes 260 codons and could encode a protein of 28,825 daltons, not 225 codons and 24,626 daltons as reported in the original article. The error was reflected in the abstr.

L1 ANSWER 27 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:52648 HCAPLUS
DOCUMENT NUMBER: 110:52648
TITLE: His-426 of the Pseudomonas aeruginosa exotoxin A is required for ADP-ribosylation of elongation factor II
AUTHOR(S): Wozniak, Daniel J.; Hsu, Leh Yeh; **Galloway, Darrell R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1988), 85(23), 8880-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Exotoxin A (ETA) is recognized as the most toxic product assocd. with the opportunistic pathogen P. aeruginosa. Identification of the amino acids in the polypeptide sequence that are required for toxin activity is crit. for vaccine development. By defining the nucleotide sequence of the structural gene of a mutant that encodes an enzymically inactive ETA (CRM 66), an essential amino acid (His-426), which is involved in the ADP-ribosyltransferase activity assocd. with functional ETA was identified. A monoclonal antibody that inhibits ETA enzymic activity in vitro fails to react with ETA variants that have a His 426 .fwdarw. Tyr substitution. Several mono-ADP-ribosylating toxins, including diphtheria and pertussis toxins, within the primary amino acid sequences carry a histidine residue that is conserved in spacing and in location with respect to other crit. residues. Anal. of the three-dimensional structure of ETA revealed that His 426 is not assocd. with the proposed NAD+ binding site. These findings should be useful for the design and construction of toxin vaccines.

L1 ANSWER 28 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:536675 HCAPLUS
DOCUMENT NUMBER: 107:136675
TITLE: A note on the stability of a family of space-periodic Beltrami flows
AUTHOR(S): **Galloway, D.**; Frisch, U.
CORPORATE SOURCE: Max-Planck-Inst. Astrophys., Garching, D-8046, Fed. Rep. Ger.
SOURCE: J. Fluid Mech. (1987), 180, 557-64

CODEN: JFLSA7; ISSN: 0022-1120
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The linear stability of flows is studied numerically, in the presence of dissipation, for the case where the perturbation has 2.pi.-periodicity as the basic flow. Above a crit. Reynolds no. (Re), the flows are unstable with a growth time that becomes comparable to the dynamic timescale of the flow as Re becomes large. The fastest-growing disturbance field is spatially intermittent, and reaches its peak intensity in features which are localized within or at the edge of regions where the undisturbed flow is chaotic, as occurs in the corresponding MHD problem.

L1 ANSWER 29 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:401681 HCAPLUS
DOCUMENT NUMBER: 107:1681
TITLE: Nucleotide sequence and characterization of toxR: a gene involved in exotoxin A regulation of Pseudomonas aeruginosa
AUTHOR(S): Wozniak, D. J.; Cram, D. C.; Daniels, C. J.; **Galloway, D. R.**
CORPORATE SOURCE: Dep. Microbiol., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Nucleic Acids Res. (1987), 15(5), 2123-35
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The P. aeruginosa gene toxR, regulates the expression of the exotoxin A (ETA) structural gene toxA. The toxR gene was transferred to a high-copy-no. plasmid (pGW28). Nucleotide sequence anal. of pGW28 revealed a 675-bp open reading frame (225 codons) which could encode for a protein of 24,626 daltons. Using S1 nuclease mapping, the toxR RNA transcript was shown to originate 20 bp upstream of the presumptive translation initiation codon. Expts. using a toxA-specific probe revealed that the toxR gene product regulates the expression of ETA at the transcriptional level.

L1 ANSWER 30 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:63362 HCAPLUS
DOCUMENT NUMBER: 104:63362
TITLE: Cloning of a gene involved in regulation of exotoxin A expression in Pseudomonas aeruginosa
AUTHOR(S): Hedstrom, R. C.; Funk, C. R.; Kaper, J. B.; Pavlovskis, O. R.; **Galloway, D. R.**
CORPORATE SOURCE: Infect. Dis. Program Cent., Nav. Med. Res. Inst., Bethesda, MD, 20814, USA
SOURCE: Infect. Immun. (1986), 51(1), 37-42
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gene was cloned from P. aeruginosa that stimulates the expression of exotoxin A. A recombinant library of genomic DNA from strain PA103 constructed with a broad-host-range plasmid vector contg. chromosomal inert fragments generated by Sau3A was used to transform the hypotoxigenic mutant strain PA103-29. A recombinant plasmid, pFHK6, was isolated from a PA103-29 transformant which displayed increased toxin prodn. From pFHK6, which contained a 20-kilobase-pair chromosomal insert, a 3-kilobase-pair XhoI fragment was isolated and subcloned into the plasmid cloning vector pVK101 to give pFHK10. In toxigenic P. aeruginosa strains contg. pFHK10, toxin expression was increased 10-fold and high levels of Fe in the

culture medium only partially inhibited the overprodn. Expression studies suggested that pFHK10 did not contain the toxin structural gene. In addn., Southern anal. with the 3-kilobase-pair XhoI fragment suggested that the putative toxin regulatory gene is common among different strains of P. aeruginosa, including previously reported nontoxigenic strains.

L1 ANSWER 31 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:18543 HCAPLUS
DOCUMENT NUMBER: 102:18543
TITLE: Herpes simplex virus types 1 and 2 homology in the region between 0.58 and 0.68 map units
AUTHOR(S): Draper, K. G.; Frink, R. J.; Devi, G. B.; Swain, M.; **Galloway, D.**; Wagner, E. K.
CORPORATE SOURCE: Dep. Mol. Biol. Biochem., Univ. California, Irvine, CA, 92717, USA
SOURCE: J. Virol. (1984), 52(2), 615-23
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The homol. between herpes simplex virus type 1 and type 2 (HSV-1 and HSV-2, resp.) DNA between 0.58 and 0.674 map units was compared by Southern and dot blot anal. with DNA of 1 type of virus as a hybridization probe against the other type. Regions of high homol. were interspersed with regions of detectably lower homol. However, only 1 region (between 0.647 and 0.653 map units) contained few or no homologous sequences. In situ RNA blot hybridization demonstrated that the mRNA species transcribed in the right-hand portion of the region are homologous between HSV-1 and HSV-2, as was previously found for the left-hand portion. A 2.7-kilobase HSV-2 transcript in the right-hand portion of the studied region was clearly that encoding HSV-2 glycoprotein C. Comparative nucleotide sequence anal. of specific regions demonstrated that homologous translational reading frames could be identified in the virus types. This anal. also demonstrated that homol. could be abruptly lost outside such reading frames. A comparison of regions of homol. with published HSV-1 transcription maps suggest that there can also be large divergence within translational reading frames. Some, but not complete, sequence homol. was seen in the putative promoter sequence for the 730-base HSV-1 mRNA mapping to the right of glycoprotein C and the corresponding HSV-2 DNA. This suggests that the rather strict conservation of promoter sequences between homologous HSV-1 and HSV-2 transcripts seen in other regions of the genome may not be a necessary feature between these virus types.

L1 ANSWER 32 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:207654 HCAPLUS
DOCUMENT NUMBER: 100:207654
TITLE: Production and characterization of monoclonal antibodies to exotoxin A from Pseudomonas aeruginosa
AUTHOR(S): **Galloway, D. R.**; Hedstrom, R. C.; Pavlovskis, O. R.
CORPORATE SOURCE: Infectious Dis. Program Cent., Nav. Med. Res. Inst., Bethesda, MD, 20814, USA
SOURCE: Infect. Immun. (1984), 44(2), 262-7
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hybridomas secreting monoclonal antibodies specific for exotoxin A from P. aeruginosa strain PA103 were derived from the fusion of spleen cells from mice immunized with: (i) purified exotoxin A, (ii) formalin-treated exotoxin A, (iii) exotoxin A covalently coupled to Sepharose 4B, or (i.v.)

P. aeruginosa-infected mice. All hybridomas were screened and selected by using an ELISA. All antibody isotypes were represented (Igs G, A, and M) as detd. by ELISA. The most productive fusions resulted from immunization with antigens coupled to an insol. matrix, such as Sepharose 4B, or by infection of mice. Several hybridomas were selected and cloned by limiting diln. The specificity of the monoclonal antibodies for exotoxin A was demonstrated by indirect immunopptn. of 125I-labeled exotoxin A followed by SDS-polyacrylamide gel electrophoresis anal. and by the immunoblotting technique. The protective ability of certain monoclonal antibodies was demonstrated in vitro by toxin neutralization in tissue culture and in vivo by prolonged survival time in the burned mouse infection model, after passive immunization. One monoclonal antitoxin displayed specificity for PA103-derived exotoxin yet failed to react with exotoxin purified from PAO-PR1 or PAO1, suggesting that structural differences exist between these exotoxins.

L1 ANSWER 33 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:152240 HCAPLUS
DOCUMENT NUMBER: 100:152240
TITLE: Toxoids of Pseudomonas aeruginosa-A: photoaffinity inactivation of purified toxin and purified toxin derivatives
AUTHOR(S): Callahan, Lynn T., III; Martinez, Douglas; Marburg, Stephen; Tolman, Richard L.; **Galloway, Darrell R.**
CORPORATE SOURCE: Res. Lab., Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Infect. Immun. (1984), 43(3), 1019-26
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB For the prepn. of greatly detoxified but highly immunogenic toxoids, 2 enzymically active, low-toxicity derivs. of P. aeruginosa exotoxin A were further inactivated by photoaffinity labeling. These derivs. were formed during toxin purifn., when a relatively crude toxin prepn. was concd. by (NH4)2SO4 pptn. and subsequently dialyzed. These derivs., designated peak-1-protein (PK-1) and peak-2 protein (PK-2) were antigenically indistinguishable from native toxin, but had isoelec. points (5.00 and 4.90, resp.) that were different from that of the native toxin (4.95). Although the enzymic activities and mol. wts. of PK-1 and PK-2 were similar to those of native toxin, their toxicities were greatly reduced (.apprx.500-fold). Photoaffinity labeling of fully active toxin A, purified by a process which limits the formation of these derivs., decreased its enzymic activity (.apprx.30-fold) and toxicity (.apprx.100-fold). Likewise, photoaffinity labeling of purified PK-1 and PK-2 decreased their enzymic activities and toxicities (.apprx.30-fold and 100-fold, resp.) and, thus, yielded toxoids that were .apprx.50,000-fold less toxic than unpurified native toxin. These toxoids were irreversibly detoxified and highly immunogenic during 9 mo of storage at 4.degree..

L1 ANSWER 34 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1984:83900 HCAPLUS
DOCUMENT NUMBER: 100:83900
TITLE: Antibody response of infected mice to outer membrane proteins of Pseudomonas aeruginosa
AUTHOR(S): Hedstrom, Richard C.; Pavlovskis, Olgerts R.; **Galloway, Darrell R.**
CORPORATE SOURCE: Nav. Med. Res. Inst., Bethesda, MD, 20814, USA
SOURCE: Infect. Immun. (1984), 43(1), 49-53

CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antibody response to outer membrane proteins of P. aeruginosa was studied in mice exptl. infected with P. aeruginosa 220. The infection consisted of an abscess established by s.c. injection of bacteria. Sera from these mice were analyzed by indirect radioimmunopptn. and immunoblot methods for the presence of antibodies to proteins of the isolated outer membrane. Sera from mice 14 days postinfection contained antibodies directed against proteins that comigrated with the major outer membrane proteins F (porin), H2, and I (lipoprotein). A 16,000-dalton protein that did not appear to be a major outer membrane protein also elicited a significant antibody response in some instances. Thus, mice, in response to infection, elicit an immunol. response to outer membrane proteins of P. aeruginosa.

L1 ANSWER 35 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:508309 HCAPLUS
DOCUMENT NUMBER: 97:108309
TITLE: Molecular and immunological characterization of human melanoma-associated antigens
AUTHOR(S): Reisfeld, R. A.; **Galloway, D. R.**; McCabe, R. P.; Morgan, Alton C., Jr.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. and Res. Found., La Jolla, CA, 92037, USA
SOURCE: Melanoma Antigens Antibodies (1982), 317-37. Editor(s): Reisfeld, Ralph A.; Ferrone, Soldano. Plenum: New York, N. Y.
CODEN: 48HEAL
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Studies suggested that melanoma-assocd. glycoprotein antigens with mol. wts. of 240,000 and 94,000 elicit host tumor responses. Expression and glycosylation of these tumor markers may be assocd. with transformation events.

L1 ANSWER 36 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:453685 HCAPLUS
DOCUMENT NUMBER: 97:53685
TITLE: An immunochemical approach to the isolation of human melanoma-associated antigens
AUTHOR(S): **Galloway, D. R.**; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, USA
SOURCE: Hum. Cancer Markers (1982), 69-88. Editor(s): Sell, Stewart; Wahren, Britta. Humana: Clifton, N. J.
CODEN: 47WDAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Two glycoprotein antigens with mol. wts. of 240,000 (240K) and 94,000 (94K) were isolated and characterized from among macromols. expressed and shed from cultured human melanoma cells. The 2 antigens could be sepd. by CM-cellulose ion-exchange chromatog. since the 240K mol. was bound at pH 5.7 and low salt concn. whereas the 94K mol. eluted under these conditions. A marked difference in their affinity for lectins led to further purifn. since the 240K mol. bound to lentil lectin and the 94K mol. to ricin lectin. This particular property together with the removal of highly immunogenic fibronectin mols. by gelatin-Sepharose chromatog. made it feasible to produce highly specific xenoantisera to the 240K and

94K antigens as the lectin-bound, fibronectin-depleted spent culture media were highly effective immunogens. Using indirect immunopptn. and subsequent anal. by SDS-polyacrylamide gel electrophoresis, the 94K mol. appeared to be a single polypeptide chain, whereas the 240K mol. was part of a larger complex, possibly linked by interchain S-S bridges. Both antigens are expressed on the surface of cultured melanoma cells from which they are readily shed in the spent culture medium. The 240K antigen has been detected only on cultured melanoma cells, whereas the 94K antigen also was expressed on a variety of carcinoma cells as well as on fetal melanocytes. Human fibroblasts and lymphoblastoid cell lines fail to express both antigens.

L1 ANSWER 37 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:179182 HCAPLUS
DOCUMENT NUMBER: 96:179182
TITLE: Carbohydrate-regulated shedding of immunochemically defined human melanoma antigens
AUTHOR(S): Morgan, A. C., Jr.; **Galloway, D. R.**; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, USA
SOURCE: Dev. Cancer Res. (1981), 5(Fundam. Mech. Hum. Cancer Immunol.), 407-21
CODEN: DCREDD; ISSN: 0163-6146
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two melanoma-assocd. antigens (MAA) of glycoprotein nature (mol. wts. 94 and 240 kilodaltons, resp.) were purified and biochem. characterized from spent melanoma culture medium. The role of the carbohydrate moiety of the glycoprotein in the expression and shedding of MAA is also described. The relation of the MAA with fetal melanocyte antigens is discussed.

L1 ANSWER 38 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:102115 HCAPLUS
DOCUMENT NUMBER: 96:102115
TITLE: Monoclonal antibodies as biochemical probes for human melanoma antigens
AUTHOR(S): Reisfeld, R. A.; Morgan, A. C.; **Galloway, D. R.**; Walker, L. E.; Bumol, T. F.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: Symp. Giovanni Lorenzini Found. (1981), 11(Monoclonal Antibodies Dev. Immunoassay), 41-52
CODEN: SGLFD9; ISSN: 0166-1167
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of monoclonal and polyclonal xenoantisera to isolate and characterize 2 melanoma-assocd. antigens (one of mol. wt. 94 K and the other of 240 K) is described.

L1 ANSWER 39 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:83861 HCAPLUS
DOCUMENT NUMBER: 96:83861
TITLE: Production and characterization of monoclonal antibody to a melanoma specific glycoprotein
AUTHOR(S): Morgan, A. C., Jr.; **Galloway, D. R.**; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA

SOURCE: Hybridoma (1981), 1(1), 27-36
CODEN: HYBRDY; ISSN: 0272-457X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An immunogen consisting of a 4M urea ext. derived from human melanoma cells (M14), that was devoid of HLA-A,B,C, HLA-DR antigens, and fibronectin was absorbed to Lens culinaris lectin-Sepharose 4B and used to immunize mice for prodn. of monoclonal antibody to a melanoma-specific glycoprotein. Screening for hybridomas secreting antibodies to melanoma-assocd. antigens was facilitated by the use of a solid-phase target antigen of chem. defined medium of melanoma cells (CDM). Use of these procedures allowed one to select 40 hybridomas secreting antibody which recognized determinants on melanoma cells not found on lymphoid cells. Further characterization of one of these hybridomas, 9.2.27, indicated that the antibody it secreted recognized a 240-kilodalton glycoprotein found on all melanoma cell lines tested but not on carcinoma, lymphoid, or fibroblastoid cultures. These results demonstrate the utility of sol. antigen prepns. devoid of strongly immunogenic non-tumor-specific mols. in the elicitation of tumor-specific antibody. Preliminary results suggest that immunogens of this kind are superior to intact melanoma cells for the prodn. of tumor-specific hybridomas.

L1 ANSWER 40 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1982:33038 HCAPLUS
DOCUMENT NUMBER: 96:33038
TITLE: Molecular profiles of human melanoma-associated antigens
AUTHOR(S): **Galloway, D. R.**; Imai, K.; Ferrone, S.; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: Fed. Proc., Fed. Am. Soc. Exp. Biol. (1981), 40(2), 231-6
CODEN: FEPRA7; ISSN: 0014-9446
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melanoma-assocd. antigens (MAA) shed into spent culture medium of intrinsically radiolabeled melanoma cells react specifically with monoclonal and polyclonal antimelanoma xenoantiserums and are represented by 2 glycoproteins with mol. wts. of 240,000 (240K) and 94K: 240K is present only on melanoma cells whereas 94K is also found on carcinoma cells and on fetal melanocytes. Both 240K and 94K have been obtained radiochemically pure by utilizing cellulose ion-exchange and antibody affinity chromatog. The 2 antigens have different charge properties, as 240K binds to CM-cellulose while 94K does not. A difference in carbohydrate moieties is also indicated since 240K binds selectively to lentil lectin and 94K to ricin lectin. Two-dimensional gel electrophoresis and tryptic peptide maps of the 2 antigens reveal distinct and characteristic profiles. Subunit structure detn. of both antigens suggests 94K to be a single chain whereas 240K appears to be a subunit of a larger mol. structure.

L1 ANSWER 41 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:494313 HCAPLUS
DOCUMENT NUMBER: 95:94313
TITLE: Topographic association of fibronectin with elastic fibers in the arterial wall. An immunohistochemical study
AUTHOR(S): Natali, P. G.; **Galloway, D.**; Nicotra, M. R.;

De Martino, C.
CORPORATE SOURCE: Regina Elena Cancer Inst., Rome, Italy
SOURCE: Connect. Tissue Res. (1981), 8(3-4), 199-204
CODEN: CVTRBC; ISSN: 0300-8207
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rabbit antibodies to human fibronectin which recognize tissue fibronectin and lack species specificity were employed to localize this mol. in the arterial wall of different animal species by indirect immunofluorescence. Fibronectin was consistently assocd. with both the inner and external aspects of the internal elastic membrane of large arteries in mammals. Only scanty staining for fibronectin was detected in collagen-rich areas of the vessel wall, i.e. adventitia. This topog. assocn. of fibronectin and internal elastic membrane was maintained in large arteries (aorta, truncus arteriosus) of all species studied, including reptiles, amphibia, and fish. Fibronectin may mediate the contraction of vessel wall structures (i.e. elastic membranes) which lack an intrinsic contractile activity.

L1 ANSWER 42 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:478266 HCAPLUS
DOCUMENT NUMBER: 95:78266
TITLE: Immunochemical delineation of an oncofetal antigen on normal and simian virus 40-transformed human fetal melanocytes
AUTHOR(S): Morgan, A. C., Jr.; **Galloway, D. R.**; Jensen, F. C.; Giovanella, B. C.; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1981), 78(6), 3834-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human melanoma cells of uveal origin shed 94,000- and 240,000-dalton glycoproteins in common with most melanoma cell lines of dermal origin. Normal human melanocytes derived from fetal uvea shed a 90,000-dalton glycoprotein that was immunol. identical with the 94,000-dalton glycoprotein of melanoma cells. Expression of this 90,000-dalton mol. was confined to fetal cells of ectodermal origin. After simian virus 40 (SV40) transformation of human fetal melanocytes, there was an apparent increase in mol. size of this component to 94,000 daltons. In contrast, the 240,000-dalton glycoprotein was not synthesized or shed by uninfected or SV40-transformed fetal melanocytes. These data suggest that the 94,000-dalton glycoprotein is an oncofetal antigen of ectodermal origin.

L1 ANSWER 43 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:137651 HCAPLUS
DOCUMENT NUMBER: 94:137651
TITLE: Serological and immunochemical analysis of the specificity of xenoantiserum 8986 elicited with hybrids between human melanoma cells and murine fibroblasts
AUTHOR(S): Imai, Kohzoh; **Galloway, Darrell R.**; Ferrone, Soldano
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: Cancer Res. (1981), 41(3), 1028-33
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Antiserums were elicited in rabbits with hybrids derived from the fusion of human melanoma cells with murine fibroblasts. Following absorption with cultured human lymphoid cells, xenoantiserum 8986 reacted with cultured human melanoma cells and other tumors of nonlymphoid origin. Rosette inhibition assays showed that the xenoantiserum reacted with structures which carry the determinants recognized by the monoclonal antibodies 165.28T and 653.25N and which are recognized by a xenoantiserum elicited with cultured human melanoma cells. SDS-polyacrylamide gel electrophoresis of the immune complexes formed by the reacting spent medium of cultured melanoma cells with xenoantiserum 8986 showed that the antiserum contains antibodies reacting with a melanoma-assocd. antigen of 240,000 mol. wt. and a melanoma-assocd. antigen of 94,000 mol. wt.

L1 ANSWER 44 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:81902 HCAPLUS
DOCUMENT NUMBER: 94:81902
TITLE: Tumor-associated antigens in spent medium of human melanoma cells: immunochemical characterization with xenoantiserums
AUTHOR(S): **Galloway, D. R.**; McCabe, R. P.; Pellegrino, M. A.; Ferrone, S.; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. and Res. Found., La Jolla, CA, 92037, USA
SOURCE: J. Immunol. (1981), 126(1), 62-6
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Xenoantisera to human melanoma cells and to partially purified melanoma-assocd. antigens were coupled to protein A-bearing Staphylococcus aureus or protein A-Sepharose and used as immunoadsorbents for the indirect immunopptn. of intrinsically radiolabeled proteins released into culture medium from various cultured human tumor and nontumor cell lines. These radiolabeled immunoppts. when analyzed by SDS-polyacrylamide gel electrophoresis revealed highly reproducible mol. profiles of proteins and glycoproteins released by various cultured tumor lines and control cells into their spent culture media. A comparison of mol. profiles together with data indicating the binding specificity of known xenoantisera produced against human melanoma cells or their exts. led to the discovery of 2 macromols. that are assocd. with human melanoma cells: a glycoprotein with a subunit mol. wt. of 240,000 (240K) and a single-chain glycoprotein of 94,000 daltons also found in assocn. with human carcinoma cells.

L1 ANSWER 45 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:63641 HCAPLUS
DOCUMENT NUMBER: 94:63641
TITLE: Human melanoma-associated antigens: role of carbohydrate in shedding and cell surface expression
AUTHOR(S): Morgan, A. C., Jr.; **Galloway, D. R.**; Imai, K.; Reisfeld, R. A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. and Res. Found., La Jolla, CA, 92037, USA
SOURCE: J. Immunol. (1981), 126(1), 365-70
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The shedding of 2 tumor-specific glycoprotein antigens from human melanoma cells into spent culture medium was selectively inhibited by nontoxic doses (0.5 .mu.g/mL) of tunicamycin, an inhibitor of N-asparagine-linked

glycosylation. The inhibition of shedding of these 2 antigens with mol. wts. of 240,000 and 94,000 is complete within 24 h after addn. of tunicamycin. During this time interval, these glycosylated cell surface antigens are replaced by their nonglycosylated forms. Removal of tunicamycin or addn. of N-acetylglucosamine restores shedding of these melanoma-assocd. antigens with initially reduced glycosylation. This same selective inhibition of shedding was obsd. with cultures adapted to grow in high doses (2.5 .mu.g/mL) of tunicamycin that otherwise killed >98% of the cells upon first exposure. In contrast to other glycoproteins found in spent culture medium of melanoma cells, the shedding of melanoma-assocd. antigens is strictly dependent of glycosylation.

L1 ANSWER 46 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1980:602560 HCAPLUS
DOCUMENT NUMBER: 93:202560
TITLE: Lack of association of serologically detectable human melanoma-associated antigens with beta2 microglobulin: serologic and immunochemical evidence
AUTHOR(S): McCabe, Richard P.; Indiveri, Francesco; **Galloway, Darrell R.**; Ferrone, Soldano; Reisfeld, Ralph A.
CORPORATE SOURCE: Dep. Mol. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: JNCI, J. Natl. Cancer Inst. (1980), 65(4), 703-7
CODEN: JJIND8; ISSN: 0198-0157
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Serol. and immunochem. assays showed that human melanoma-assocd. antigens (MAA) identified with operationally specific xenoantiserums were neither spatially nor structurally assocd. with .beta.2-microglobulin (.beta.2-.mu.), the light chain of the HLA-A,B antigen mol. complex; i.e., cultured melanoma cells coated with a specific anti-.beta.2-.mu. xenoantiserum maintained their reactivity with anti-MAA xenoantiserum. Furthermore, sol. MAA were not bound by a .beta.2-.mu. immunoadsorbent. MAA were shed into the culture medium of melanoma cells and then were immunopptd. with specific anti-MAA xenoantiserums; when analyzed by SDS-polyacrylamide gel electrophoresis, they appeared as 2 distinct structures with mol. wts. of 240,000 and 94,000 but comprised no structure with the characteristic 12,000 mol. wt. of .beta.2-.mu.. Conversely, immunoppts. obtained by the reaction of spent culture medium of [3H]valine-labeled melanoma cells with anti-.beta.2-.mu. xenoantiserum had the 12,000-mol.-wt. component but no structures with the mol. wts. established for MAA. Thus, the data refute the contention that serol. detectable MAA have a mol. structure similar to that of HLA antigens.

L1 ANSWER 47 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1979:554016 HCAPLUS
DOCUMENT NUMBER: 91:154016
TITLE: Reconstitution of binding protein-dependent ribose transport in spheroplasts of Escherichia coli K-12
AUTHOR(S): **Galloway, Darrell R.**; Furlong, Clement E.
CORPORATE SOURCE: Dep. Biochem., Univ. California, Riverside, CA, 92521, USA
SOURCE: Arch. Biochem. Biophys. (1979), 197(1), 158-62
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purified E. coli K-12 ribose-binding protein was used to reconstitute the high-affinity ribose transport system in spheroplasts derived from

ribose-induced cells. It was not possible to reconstitute ribose transport in spheroplasts derived from uninduced cells or from transport-neg. mutant strains, suggesting that .gtoreq.1 addnl. inducible components are required for binding protein-dependent ribose transport. It was possible to reconstitute transport in a ribokinase-deficient mutant which constitutively transports but does not utilize ribose.

L1 ANSWER 48 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1979:69017 HCAPLUS
DOCUMENT NUMBER: 90:69017
TITLE: The relationship of the ribose-binding protein to transport and chemotaxis in Escherichia coli
AUTHOR(S): **Galloway, Darrell Ray**
CORPORATE SOURCE: Univ. California, Riverside, Calif., USA
SOURCE: (1978) 148 pp. Avail.: Univ. Microfilms Int., Order No. 7821349
From: Diss. Abstr. Int. B 1978, 39(5), 2270
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L1 ANSWER 49 OF 49 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1978:34294 HCAPLUS
DOCUMENT NUMBER: 88:34294
TITLE: The role of ribose-binding protein in transport and chemotaxis in Escherichia coli K12
AUTHOR(S): **Galloway, Darrell R.**; Furlong, Clement E.
CORPORATE SOURCE: Dep. Biochem., Univ. California, Riverside, Calif., USA
SOURCE: Arch. Biochem. Biophys. (1977), 184(2), 496-504
CODEN: ABBIA4
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ribose-binding protein of E. coli (Willis, R. C.; Furlong, C. E., 1974) was a required common receptor component for high-affinity ribose transport and for chemotaxis toward this attractant. Mutants devoid of the ribose-binding protein lack high-affinity ribose transport and do not respond chemotactically to this sugar, whereas the response to other attractants is normal. Eight independently isolated ribose-pos. revertant strains regained the binding protein, high-affinity ribose transport, and ribose chemotaxis. One revertant that grows slowly on ribose as a sole C source did not regain the binding protein, high-affinity transport, or ribose chemotaxis.

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                 OR "GALLOWAY DARRELL RAY"/AU)
L2             0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("MATECZUN ALFRED"/AU OR
                 "MATECZUN ALFRED J"/AU OR "MATECZUN ALFRED J"/IN) NOT L1


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L3          258 SEA FILE=REGISTRY ABB=ON  PLU=ON  ANTHRACIS OR ANTHRAX
L4           19 SEA FILE=REGISTRY ABB=ON  PLU=ON  LETHAL(L)FACTOR
L5           31 SEA FILE=REGISTRY ABB=ON  PLU=ON  PROTECTIVE(W)ANTIGEN
L7         3869 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR LETHAL(L)FACTOR
L8          992 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR PROTECTIVE(W)ANTIGEN
L9         1650 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR ?ANTHRACIS OR ?ANTHRAX
L10         193 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9(L)L7
L11         147 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L8
L12          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (VACCIN? OR IMMUNIZ?)

L13          36 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 NOT L1


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L13  ANSWER 1 OF 36  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:669902  HCAPLUS
DOCUMENT NUMBER:          135:299791
TITLE:                    Hydrophobic Residues Phe552, Phe554, Ile562, Leu566,
                          and Ile574 Are Required for Oligomerization of Anthrax
                          Protective Antigen
AUTHOR(S):                Ahuja, Nidhi; Kumar, Praveen; Bhatnagar, Rakesh
CORPORATE SOURCE:         Centre for Biotechnology, Jawaharlal Nehru University,
                          New Delhi, 110067, India
SOURCE:                   Biochem. Biophys. Res. Commun. (2001), 287(2), 542-549
                          CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER:                Academic Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Anthrax protective antigen (PA) plays a
     central role in facilitating the entry of active toxin components, namely,
     lethal factor and edema factor, into the
     cells.  PA is also the main immunogen of both human and veterinary
     vaccine against anthrax.  During host cell intoxication,
     protective antigen binds to the receptors on cell
     surface, gets proteolytically activated, oligomerizes to form a heptamer
     and binds to lethal factor or edema factor.
     The complex, formed by binding of lethal factor or
     edema factor to oligomerized PA, is internalized by
     receptor-mediated endocytosis.  Acidification of the endosome results in
     the insertion of the heptamer into the membrane, thereby forming a pore
     through which lethal factor or edema factor
     can translocate into the cytosol.  In this study we have identified
     hydrophobic residues, Phe552, Phe554, Ile562, Leu566, and Ile574, which
     are required for oligomerization of anthrax protective
     antigen.  Mutation of these conserved residues to alanine impaired
     the oligomerization of protective antigen.
     Consequently, these mutants became nontoxic in combination with
     lethal factor and edema factor.  Therapeutic
     importance of these mutants and their potential as vaccine
     candidates is discussed.  (c) 2001 Academic Press.
REFERENCE COUNT:          28
REFERENCE(S):             (1) Barth, H; J Biol Chem 2000, V275, P18704 HCAPLUS
                          (2) Barth, H; J Biol Chem 2001, V276, P10670 HCAPLUS
                          (3) Batra, S; Biochem Biophys Res Commun 2001, V281,
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P186 HCAPLUS
(4) Bhatnagar, R; Cell Signal 1999, V11(2), P111 HCAPLUS
(5) Bhatnagar, R; Infect Immun 1989, V57, P2107 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:563312 HCAPLUS
DOCUMENT NUMBER: 135:302477
TITLE: Rapid Purification of Recombinant Anthrax-**Protective Antigen** under Nondenaturing Conditions
AUTHOR(S): Ahuja, Nidhi; Kumar, Praveen; Bhatnagar, Rakesh
CORPORATE SOURCE: Centre for Biotechnology, Jawaharlal Nehru University, New Delhi, 110067, India
SOURCE: Biochem. Biophys. Res. Commun. (2001), 286(1), 6-11
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Anthrax-protective antigen** is the central moiety of the **anthrax** toxin complex that mediates the entry of the other two toxin components, **lethal factor** and edema **factor** into the cells. It is also the main immunogen of the cell-free **vaccine** against **anthrax**. However, in addn. to PA, the **vaccine** contains trace amts. of other culture-derived proteins that contribute to the side effects of the **vaccine** like pain, edema, erythrema, etc. Thus there is a need to develop high-resoln. purifn. methods to purify PA to homogeneity. In this study we have presented a purifn. strategy for rapid purifn. of recombinant **protective antigen** under nondenaturing conditions, which ensures that not only biol. activity but also the conformational integrity of immunol. epitopes is well-preserved. The protein was purified to homogeneity in a two-step purifn. procedure that takes just 6 h for completion. Three milligrams of recombinant **protective antigen** obtained from 1-L culture was comparable to B. **anthracis protective antigen** in terms of functional and biol. activity. Moreover, the immunogenicity elicited by the purified protein in mice was also studied. The studies reported here are part of continuing research that aims to provide a safe and efficacious alternative to the current **vaccine** against **anthrax**. (c) 2001 Academic Press.
REFERENCE COUNT: 22
REFERENCE(S): (1) Batra, S; Biochem Biophys Res Commun 2001, V281(1), P186 HCAPLUS
(2) Bhatnagar, R; Cell Signal 1999, V11(2), P111 HCAPLUS
(3) Bhatnagar, R; Infect Immun 1989, V57, P2107 HCAPLUS
(4) Gupta, P; Prot Exp Purif 1999, V16, P369 HCAPLUS
(5) Iacono-Connors, L; Infect Immun 1990, V58, P366 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:470950 HCAPLUS
DOCUMENT NUMBER: 135:194200
TITLE: The role of antibodies to Bacillus anthracis and

anthrax toxin components in inhibiting the early stages of infection by anthrax spores
AUTHOR(S): Welkos, Susan; Little, Stephen; Friedlander, Arthur; Fritz, David; Fellows, Patricia
CORPORATE SOURCE: Divisions of Bacteriology, US Army Medical Research Institute of Infectious Diseases, Frederick, MD, 21702-5011, USA
SOURCE: Microbiology (Reading, U. K.) (2001), 147(6), 1677-1685
CODEN: MROBEO; ISSN: 1350-0872
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Vaccines** which are efficacious against **anthrax**, such as the human **vaccine, Anthrax Vaccine** Absorbed (AVA), contain the **protective antigen** (PA) component of the **anthrax** toxins as the major protective immunogen. Although AVA protects against inhalational **anthrax**, the immune responses to and role in protection of PA and possibly other antigens have yet to be fully elucidated. Sera from animals **immunized** with a toxin-producing, unencapsulated live **vaccine** strain of Bacillus **anthracis** have been reported to have anti-spore activities assocd. with the antitoxin humoral response. The authors performed studies to det. whether anti-PA antibody (Ab)-contg. prepns. stimulated spore uptake by phagocytes and suppressed the germination of spores in vitro. AVA- and PA-immune sera from several species enhanced the phagocytosis by murine peritoneal macrophages of spores of the virulent Ames and the Sterne **vaccine** strains. Antitoxin Abs appeared to contribute significantly, although not solely, to the enhanced uptake. Rabbit antisera to PA purified from either Sterne or a PA-producing pX01-cured recombinant, affinity-purified anti-PA IgG, and monkey antisera to AVA were used to assess the role of anti-PA Abs. Rabbit anti-PA Abs promoted the uptake of spores of the PA-producing strains Sterne, Ames and RP42, a mutant of Sterne producing only PA, but not of the pX01-.DELTA.Sterne-1 strain, .DELTA.Ames strain, or RP4, a mutant of Sterne with deletions in the loci encoding PA and the edema **factor** (EF) toxin component and producing only the **lethal factor** toxin component. Rabbit anti-PA and monkey anti-AVA Abs also significantly inhibited spore germination in vitro compared to preimmune serum or medium. Spore-assocd. proteins recognized by anti-PA Abs were detected by electron microscopy and confirmed by immunoblotting of spore coat exts. Thus, the anti-PA Ab-specific immunity induced by AVA has anti-spore activity and might have a role in impeding the early stages of infection with B. **anthracis** spores.
REFERENCE COUNT: 35
REFERENCE(S): (1) Aronson, A; Bacteriol Rev 1976, V40, P360 HCAPLUS
(2) Barnes, J; Br J Exp Pathol 1947, V28, P385 HCAPLUS
(3) Beaman, T; J Bacteriol 1971, V107, P320 HCAPLUS
(5) Dixon, T; Cell Microbiol 2000, V2, P453 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:318771 HCAPLUS
DOCUMENT NUMBER: 135:91214
TITLE: Anthrax-toxin-mediated delivery of a 19 kDa antigen of Mycobacterium tuberculosis into the cytosol of mammalian cells
AUTHOR(S): Mehra, Varsha; Khanna, Hemant; Chandra, Ramesh; Singh,

Yogendra
CORPORATE SOURCE: Centre for Biochemical Technology, Delhi, 110007, India
SOURCE: Biotechnol. Appl. Biochem. (2001), 33(2), 71-74
CODEN: BABIEC; ISSN: 0885-4513
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PA63, the proteolytically activated 63 kDa fragment of **protective antigen** (PA, 83 kDa), mediates translocation of **lethal factor** (LF) and edema **factor** into the cytosol. The N-terminal 254 amino acids of LF (LFn) are required for binding to PA63 and mediating translocation of active ligands fused to either the N- or C-terminus. Here we report translocation of a 19 kDa antigen of Mycobacterium tuberculosis into the cytosol of mammalian cells when fused to the C-terminus of LFn (LFn-19kDa). The fusion protein was non-toxic to J774A.1 macrophage cells in combination with PA and retained the ability to bind to PA63 when incubated with Chinese hamster ovary KI cells. The data show the efficacy of **anthrax** toxin to mediate translocation of M. tuberculosis antigens into the cytosol of mammalian cells and may prove useful in delivering proteins and peptides carrying immunodominant mycobacterial antigens into the cytosol.
REFERENCE COUNT: 17
REFERENCE(S):
(1) Arora, N; Infect Immun 1994, V62, P4955 HCAPLUS
(2) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
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(5) Benson, E; Biochemistry 1998, V37, P3941 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:304534 HCAPLUS
DOCUMENT NUMBER: 135:106319
TITLE: Constitutive Expression of **Protective Antigen** Gene of Bacillus anthracis in Escherichia coli
AUTHOR(S): Chauhan, Vibha; Singh, Aparna; Waheed, S. Mohsin; Singh, Samer; Bhatnagar, Rakesh
CORPORATE SOURCE: Centre For Biotechnology, Jawaharlal Nehru University, New Delhi, 110067, India
SOURCE: Biochem. Biophys. Res. Commun. (2001), 283(2), 308-315
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fatal bacterial infection caused by inhalation of the Bacillus **anthracis** spores results from the synthesis of protein toxins-**protective antigen** (PA), **lethal factor** (LF), and edema **factor** (EF)-by the bacterium. PA is the target-cell binding protein and is common to the two effector mols., LF and EF, which exert their toxic effects once they are translocated to the cytosol by PA. PA is the major component of **vaccines** against **anthrax** since it confers protective immunity. The large-scale prodn. of recombinant protein-based **anthrax vaccines** requires overexpression of the PA protein. We have constitutively expressed the **protective antigen** protein in E. coli DH5.alpha. strain. We have found no increase in degrdn. of PA when the protein is constitutively expressed and no plasmid instability was obsd.

inside the expressing cells. We have also scaled up the expression by bioprocess optimization using batch culture technique in a fermentor. The protein was purified using metal-chelate affinity chromatog. Approx. 125 mg of recombinant **protective antigen** (rPA) protein was obtained per L of batch culture. It was found to be biol. and functionally fully active in comparison to PA protein from Bacillus **anthracis**. This is the first report of constitutive overexpression of **protective antigen** gene in E. coli.
(c) 2001 Academic Press.

REFERENCE COUNT: 50
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:790362 HCAPLUS
DOCUMENT NUMBER: 133:361905
TITLE: Topical genetic **immunization**
INVENTOR(S): Tang, De-Chu C.; Marks, Donald H.; Curiel, David T.; Shi, Zhongkai; Van Kampen, Kent R.
PATENT ASSIGNEE(S): The UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066179	A1	20001109	WO 2000-US12001	20000503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-132216 P 19990503
US 2000-533149 A 20000323

AB The authors disclose methods of non-invasive, topical, genetic **immunization** which induce a systemic immune response. In one example, an adenovirus vector expressing human carcinoembryonic antigen was absorbed to the skin of mice after depilation. These mice developed an antibody response to CEA and were able to survive challenge with a CEA-bearing tumor. In a second example, pigtail macaques received an adenovirus vector expressing influenza hemagglutinin. Four weeks following non-invasive **immunization**, an IgG response to

influenza virus was demonstrable. Addnl., an immune response was obtainable against model antigens when delivered either as a DNA/liposome or a DNA/adenovirus complex.

REFERENCE COUNT: 9

REFERENCE(S):
(1) Carson; US 5679647 A 1997 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:685426 HCAPLUS
DOCUMENT NUMBER: 133:333663
TITLE: **Protective antigen**-mediated antibody response against a heterologous protein produced in vivo by Bacillus anthracis
AUTHOR(S): Brossier, Fabien; Weber-Levy, Martine; Mock, Michele; Sirard, Jean-Claude
CORPORATE SOURCE: Unite Toxines et Pathogenie Bacteriennes, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Infect. Immun. (2000), 68(10), 5731-5734
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacillus **anthracis** secretes a **lethal** toxin composed of two proteins, the **lethal factor** (LF) and the **protective antigen** (PA), which interact within the host or in vitro at the surfaces of eukaryotic cells. **Immunization** with attenuated B. **anthracis** strains induces an antibody response against PA and LF. The LF-specific response is potentiated by the binding of LF to PA. In this study, the authors investigated the capacity of PA to increase the antibody response against a foreign antigen. The authors constructed a chimeric gene encoding the PA-binding part of LF (LF254) fused to the C fragment of tetanus toxin (ToxC). The construct was introduced by allelic exchange into the locus encoding LF. Two recombinant B. **anthracis** strains secreting the hybrid protein LF254-ToxC were generated, one in a PA-producing background and the other in a PA-deficient background. Mice were **immunized** with spores of the strains, and the humoral response and protection against tetanus toxin were assessed. The B. **anthracis** strain producing both PA and LF254-ToxC induced significantly higher antibody titers and provided better protection against a **lethal** challenge with tetanus toxin than did its PA-deficient counterpart. Thus, PA is able to potentiate protective immunity against a heterologous antigen, demonstrating the potential of B. **anthracis** recombinant strains for use as live **vaccine** vehicles.

REFERENCE COUNT: 32

REFERENCE(S):
(1) Arora, N; Infect Immun 1994, V62, P4955 HCAPLUS
(2) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:642259 HCAPLUS
DOCUMENT NUMBER: 133:295021
TITLE: Anthrax toxin-mediated delivery of cholera toxin-A subunit into the cytosol of mammalian cells
AUTHOR(S): Sharma, Manju; Khanna, Hemant; Arora, Naveen; Singh, Yogendra
CORPORATE SOURCE: Centre for Biochemical Technology, Delhi, 110007, India
SOURCE: Biotechnol. Appl. Biochem. (2000), 32(1), 69-72
CODEN: BABIEC; ISSN: 0885-4513
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **protective antigen** (PA) component of **anthrax** toxin mediates delivery of either **lethal factor** (LF) or edema **factor** into the cytosol of mammalian cells. The N-terminal domain of LF1-254 (amino acids 1-254 of LF) binds to PA and, when fused to heterologous proteins, delivers such proteins into the cytosol. In the present study, we fused the catalytic subunit of cholera toxin (CT-A) with LF1-254 and showed that the fusion protein LF1-254-CT-A retains ADP-ribosylation activity in soln. and increased intracellular cAMP levels in J774A.I macrophage cells when added together with PA. A mutant fusion protein, in which arginine-7 of CT-A was replaced with lysine, did not show ADP-ribosylation activity in soln. and failed to increase cAMP levels in macrophage cells. The data show that LF1-254-CT-A retains its catalytic activity in soln. as well as when translocated into the cytosol of eukaryotic cells via an alternative pathway to the GM1 receptor used by CT.
REFERENCE COUNT: 24
REFERENCE(S): (1) Arora, N; Infect Immun 1994, V62, P4955 HCAPLUS
(2) Arora, N; J Biol Chem 1992, V267, P15542 HCAPLUS
(3) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
(4) Arora, N; J Biol Chem 1994, V269, P26165 HCAPLUS
(5) Ballard, J; Proc Natl Acad Sci U S A 1996, V93, P12531 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:494505 HCAPLUS
DOCUMENT NUMBER: 133:221323
TITLE: Genetically modified anthrax lethal toxin safely delivers whole HIV protein antigens into the cytosol to induce T cell immunity
AUTHOR(S): Lu, Yichen; Friedman, Rachel; Kushner, Nicholas; Doling, Amy; Thomas, Lawrence; Touzjian, Neal; Starnbach, Michael; Lieberman, Judy
CORPORATE SOURCE: Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, MA, 02115, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (2000), 97(14), 8027-8032
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacillus anthrax lethal toxin can be engineered to deliver foreign proteins to the cytosol for antigen presentation to CD8 T cells. **Vaccination** with modified toxins carrying 8-9 amino acid peptide epitopes induces protective immunity in mice. To evaluate whether large

protein antigens can be used with this system, recombinant constructs encoding several HIV antigens up to 500 amino acids were produced. These candidate HIV **vaccines** are safe in animals and induce CD8 T cells in mice. Constructs encoding gag p24 and nef stimulate gag-specific CD4 proliferation and a secondary cytotoxic T lymphocyte response in HIV-infected donor peripheral blood mononuclear cells in vitro. These results lay the foundation for future clin. **vaccine** studies.

REFERENCE COUNT: 27
REFERENCE(S):
(1) Ballard, J; Infect Immun 1998, V66, P615 HCAPLUS
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(4) Brodie, S; Nat Med 1999, V5, P34 HCAPLUS
(5) Culmann, B; J Immunol 1991, V146, P1560 HCAPLUS
(6) Duesbery, N; Science 1998, V280, P734 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:339086 HCAPLUS
DOCUMENT NUMBER: 133:249630
TITLE: Characterization of Bacillus anthracis strains used for **vaccination**
AUTHOR(S): Cataldi, A.; Mock, M.; Bentancor, L.
CORPORATE SOURCE: Biotechnology Institute, Moron, 1708, Argent.
SOURCE: J. Appl. Microbiol. (2000), 88(4), 648-654
CODEN: JAMIFK; ISSN: 1364-5072
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three Bacillus anthracis strains, formerly used as anti-anthrax **vaccine** strains in Argentina, were characterized from genetic and pathogenic perspectives. Southern blotting and PCR with pXO1 and pXO2 probes and primers, as well as pathogenicity and protection tests in guinea pigs and mice, were performed. Two of the B. anthracis strains contained both pXO1 and pXO2 plasmids, as did the fully virulent strains, while the third was a Sterne-type strain (pXO1+, pXO2-). The three strains were, however, markedly less pathogenic than a wild-type virulent strain. The methodol. applied here may be used to characterize other B. anthracis strains.

REFERENCE COUNT: 21
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:213551 HCAPLUS
DOCUMENT NUMBER: 132:344326
TITLE: Role of toxin functional domains in anthrax pathogenesis
AUTHOR(S): Brossier, Fabien; Weber-Levy, Martine; Mock, Michele; Sirard, Jean-Claude
CORPORATE SOURCE: Unite Toxines et Pathogenie Bacteriennes, Institut Pasteur (CNRS URA 1858), Paris, 75724, Fr.

SOURCE: Infect. Immun. (2000), 68(4), 1781-1786
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors investigated the role of the functional domains of **anthrax** toxins during infection. Three proteins produced by Bacillus **anthracis**, the **protective antigen** (PA), the **lethal factor** (LF), and the edema **factor** (EF), combine in pairs to produce the **lethal** (PA+LF) and edema (PA+EF) toxins. A genetic strategy was developed to introduce by allelic exchange specific point mutations or in-frame deletions into B. **anthracis** toxin genes, thereby impairing either LF metalloprotease or EF adenylate cyclase activity or PA functional domains. In vivo effects of toxin mutations were analyzed in an exptl. infection of mice. A tight correlation was obsd. between the properties of **anthrax** toxins delivered in vivo and their in vitro activities. The synergic effects of the **lethal** and edema toxins resulted purely from their enzymic activities, suggesting that in vivo these toxins may act together. The PA-dependent antibody response to LF induced by **immunization** with live B. **anthracis** was used to follow the in vivo interaction of LF and PA. The authors found that the binding of LF to PA in vivo was necessary and sufficient for a strong antibody response against LF, whereas neither LF activity nor binding of **lethal** toxin complex to the cell surface was required. Mutant PA proteins were cleaved in mice sera. Thus, the authors' data provide evidence that, during **anthrax** infection, PA may interact with LF before binding to the cell receptor. Immunoprotection studies indicated that the strain producing detoxified LF and EF, isogenic to the current live **vaccine** Sterne strain, is a safe candidate for use as a **vaccine** against **anthrax**.

REFERENCE COUNT: 42
REFERENCE(S): (3) Brossier, F; C R Soc Biol 1998, V192, P437 HCAPLUS
(4) Brossier, F; Infect Immun 1999, V67, P964 HCAPLUS
(5) Duesbery, N; Science 1998, V280, P734 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:194552 HCAPLUS
DOCUMENT NUMBER: 133:13577
TITLE: Optimized Production and Purification of Bacillus **anthracis Lethal Factor**
AUTHOR(S): Park, Sukjoon; Leppla, Stephen H.
CORPORATE SOURCE: Oral Infection and Immunity Branch, National Institute of Dental and Craniofacial Research, National Institute of Health, Bethesda, MD, 20892, USA
SOURCE: Protein Expression Purif. (2000), 18(3), 293-302
CODEN: PEXPEJ; ISSN: 1046-5928
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacillus **anthracis lethal factor** (LF) is a 90-kDa zinc metalloprotease that plays an important role in the virulence of the organism. LF has previously been purified from Escherichia coli and Bacillus **anthracis**. The yields and purities of these prepns. were inadequate for crystal structure detn. In this study, the genes encoding wild-type LF and a mutated, inactive LF (LF-E687C) were

placed in an E. coli-Bacillus shuttle vector so that LF was produced with the **protective antigen** (PA) signal peptide at its N-terminus. The resulting vectors, pSJ115 and pSJ121, express wild-type and mutated LF fusion proteins, resp. Expression of the LF genes is under the control of the PA promoter and, during secretion, the PA signal peptide is cleaved to release the 90-kDa LF proteins. The wild-type and mutated LF proteins were purified from the culture medium using three chromatog. steps (Phenyl-Sepharose, Q-Sepharose, and hydroxyapatite). The purified proteins were greater than 95% pure and yields (20-30 mg/L) were higher than those obtained in other expression systems (1-5 mg/L). These proteins have been crystd. and are being used to solve the crystal structure of LF. Their potential use in **anthrax vaccines** is also discussed. (c) 2000 Academic Press.

REFERENCE COUNT: 36

REFERENCE(S):
(1) Bartkus, J; Infect Immun 1989, V57, P2295 HCAPLUS
(2) Bragg, T; Gene 1989, V81, P45 HCAPLUS
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(4) Dai, Z; Mol Microbiol 1995, V16, P1171 HCAPLUS
(5) Duesbery, N; Science 1998, V280, P734 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:412210 HCAPLUS

DOCUMENT NUMBER: 131:183604

TITLE: Cytotoxic T-lymphocyte epitopes fused to anthrax toxin induce protective antiviral immunity

AUTHOR(S): Doling, Amy M.; Ballard, Jimmy D.; Shen, Hao; Krishna, Kaja Murali; Ahmed, Rafi; Collier, R. John; Starbach, Michael N.

CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Infect. Immun. (1999), 67(7), 3290-3296
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have investigated the use of the **protective antigen** (PA) and **lethal factor** (LF) components of **anthrax** toxin as a system for in vivo delivery of cytotoxic T-lymphocyte (CTL) epitopes. During intoxication, PA directs the translocation of LF into the cytoplasm of mammalian cells. Here we demonstrate that antiviral immunity can be induced in BALB/c mice **immunized** with PA plus a fusion protein contg. the N-terminal 255 amino acids of LF (LFn) and an epitope from the nucleoprotein (NP) of lymphocytic choriomeningitis virus. We also demonstrate that BALB/c mice **immunized** with a single LFn fusion protein contg. NP and listeriolysin O protein epitopes in tandem mount a CTL response against both pathogens. Furthermore, we show that NP-specific CTL are primed in both BALB/c and C57BL/6 mice when the mice are **immunized** with a single fusion contg. two epitopes, one presented by Ld and one presented by Db. The data presented here demonstrate the versatility of the **anthrax** toxin delivery system and indicate that this system may be used as a general approach to **vaccinate** outbred populations against a variety of pathogens.

REFERENCE COUNT: 37

REFERENCE(S):
(2) Ahmed, R; Science 1996, V272, P54 HCAPLUS
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(5) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:248393 HCAPLUS
DOCUMENT NUMBER: 131:69887
TITLE: Purification of the **protective antigen** from Bacillus anthracis
AUTHOR(S): Cho, Soung-Kun; Park, Jeung-Moon; Choi, Young-Keel; Kim, Seong-Joo; Chai, Young-Gyu
CORPORATE SOURCE: National Livestock Research Institute, Korean Microbiological Lab., Ltd., S. Korea
SOURCE: Taehan Misaengmul Hakhoechi (1998), 33(6), 589-594
CODEN: TMHCDX; ISSN: 0253-3162
PUBLISHER: Korean Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: Korean
AB **Anthrax** toxin consists of three sep. proteins, **protective antigen** (PA), edema **factor** (EF), and **lethal factor** (LF). PA binds to the receptor on mammalian cells and facilitates translocation of EF or LF into its cytosol. PA is the primary component of **anthrax vaccines**. In this study we purified PA from culture filtrates of Bacillus **anthracis**. The purifn. involved sequential chromatog. through hydroxylapatite, DEAE-Sepharose CL-4B, followed by Mono-Q. The purified PA was judged to be homogeneous on SDS-PAGE, and consisted of a single polypeptide chain with a relative mol. wt. of 85,000.

L13 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:43514 HCAPLUS
DOCUMENT NUMBER: 130:250868
TITLE: Protection against anthrax toxin by **vaccination** with a DNA plasmid encoding anthrax **protective antigen**
AUTHOR(S): Gu, Mi-Li; Leppla, Stephen H.; Klinman, Dennis M.
CORPORATE SOURCE: Section of Retroviral Immunology, Division of Viral Products, Center for, Evaluation and Research, Food and Drug Administration, MD, USA
SOURCE: Vaccine (1998), Volume Date 1999, 17(4), 340-344
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A DNA **vaccine** encoding the immunogenic and biol. active portion of **anthrax protective antigen** (PA) was constructed. Spleen cells from BALB/c mice **immunized** i.m. with this **vaccine** were stimulated to secrete IFN.gamma. and IL-4 when exposed to PA in vitro. **Immunized** mice also mounted a humoral immune response dominated by IgG1 anti-PA antibody prodn., the subclass previously shown to confer protection against **anthrax** toxin. A 1:100 diln. of serum from these animals protected cells in vitro against cytotoxic concns. of PA. Moreover, 7/8 mice **immunized** three times with the PA DNA **vaccine** were protected against **lethal** challenge with a combination of **anthrax protective antigen** plus **lethal factor**

REFERENCE COUNT: 27
REFERENCE(S): (2) Coulson, N; Vaccine 1994, V12, P1395 HCAPLUS
(4) Gordon, V; Infect Immun 1995, V63, P82 HCAPLUS

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(6) Ivins, B; Vaccine 1995, V13, P1779 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:27954 HCAPLUS
DOCUMENT NUMBER: 130:77075
TITLE: Targetting and uptake of DNA by animal cells by receptor-mediated endocytosis using fusion protein of toxins and DNA-binding proteins
INVENTOR(S): Grandi, Guido
PATENT ASSIGNEE(S): Chiron S.P.A., Italy
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9859065	A1	19981230	WO 1998-IB1005	19980618

W: JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: GB 1997-13122 19970620

AB A method of using receptor-mediated endocytosis to increase the efficiency of DNA uptake by eukaryotic cells is described. The method uses fusion proteins of receptor-binding domains of toxins, therefore lacking the domains necessary for toxic activity, and DNA-binding domains. These fusion proteins are taken up by the receptor for the toxin and the DNA it is bound to is incorporated into the endosome. When the endosome is internalized, the complex is released and the protein stripped from the DNA leaving it free to become part of the host cell genome. A fusion protein of the heat-labile enterotoxin of Escherichia coli and the histone H1-like protein of Bordetella pertussis was prepd. by expression of the cloned gene. The protein was shown to retain DNA binding activity. Similarly, a fusion protein of diphtheria toxin and GAL4 was shown to have DNA binding and to retain the normal binding of the toxin to Vero cells. The fusion protein was also rapidly internalized by Vero cells.

REFERENCE COUNT: 6
REFERENCE(S): (1) Dana Farber Cancer Inst Inc; WO 9522618 A 1995 HCAPLUS
(2) Maxim Pharmaceuticals; WO 9705267 A 1997 HCAPLUS
(3) Miles Inc; WO 9404696 A 1994 HCAPLUS
(4) Starnbach Michael N; WO 9613599 A 1997 HCAPLUS
(5) Starnbach Michel N; WO 9723236 A 1997 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:649596 HCAPLUS
DOCUMENT NUMBER: 130:23854
TITLE: Anthrax toxin as a molecular tool for stimulation of cytotoxic T lymphocytes: disulfide-linked epitopes, multiple injections, and role of CD4+ cells
AUTHOR(S): Ballard, Jimmy D.; Collier, R. John; Starnbach, Michael N.
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics,

Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Infect. Immun. (1998), 66(10), 4696-4699
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously demonstrated that **anthrax** toxin-derived proteins, **protective antigen** (PA) and the amino-terminal portion of **lethal factor** (LFn), can be used in combination to deliver heterologous mols. to the cytosol of mammalian cells. In this study we examd. the ability of an LFn-peptide disulfide-linked heterodimer to prime cytotoxic T lymphocytes (CTL) in the presence of PA. A mutant of LFn that contains a carboxy-terminal reactive cysteine was generated. This form of LFn could be oxidized with a synthetic cysteine contg. peptide to form a heterodimer of the protein and peptide. Mice injected with the heterodimer plus PA mounted a peptide-specific CTL response, indicating that this mol. functioned similarly to the genetically fused forms used previously. We also report the results of an anal. of two aspects of this system important for the development of exptl. **vaccines**. First, CD4 knockout mice were unable to generate a CTL response when treated with PA plus an LFn-epitope fusion protein, suggesting that CD4+ helper responses are essential for stimulating specific CTL with the PA-LFn system. Second, we now show that primary injection with this system does not generate any detectable antibody response to the **vaccine** components and that prior **immunization** has no effect on priming a CTL response to an unrelated epitope upon subsequent injection.
REFERENCE COUNT: 17
REFERENCE(S): (2) Ahmed, R; Science 1996, V272, P54 HCAPLUS
(3) Arora, N; Infect Immun 1994, V62, P4955 HCAPLUS
(4) Ballard, J; Infect Immun 1998, V66, P615 HCAPLUS
(5) Ballard, J; Proc Natl Acad Sci USA 1996, V93, P12531 HCAPLUS
(7) Hanna, P; Mol Med 1994, V1, P7 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:414029 HCAPLUS
DOCUMENT NUMBER: 129:147828
TITLE: Study of **immunization** against anthrax with the purified recombinant **protective antigen** of Bacillus anthracis
AUTHOR(S): Singh, Yogendra; Ivins, Bruce E.; Leppla, Stephen H.
CORPORATE SOURCE: Centre for Biochemical Technology, Delhi, 110 007, India
SOURCE: Infect. Immun. (1998), 66(7), 3447-3448
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Protective antigen** (PA) of **anthrax** toxin is the major component of human **anthrax vaccine**. Currently available human **vaccines** in the United States and Europe consist of alum-pptd. supernatant material from cultures of toxigenic, nonencapsulated strains of Bacillus **anthracis**. **Immunization** with these **vaccines** requires several boosters and occasionally causes local pain and edema. We previously described the biol. activity of a nontoxic mutant of PA expressed in Bacillus subtilis. In the present study, we evaluated the efficacy of the

purified mutant PA protein alone or in combination with the **lethal factor** and edema **factor** components of **anthrax** toxin to protect against **anthrax**. Both mutant and native PA prepns. elicited high anti-PA titers in Hartley guinea pigs. Mutant PA alone and in combination with **lethal factor** and edema **factor** completely protected the guinea pigs from B. **anthracis** spore challenge. The results suggest that the mutant PA protein may be used to develop an effective recombinant **vaccine** against **anthrax**.

L13 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:197415 HCAPLUS
DOCUMENT NUMBER: 128:256376
TITLE: Targeting antigens to the MHC class I processing pathway with anthrax toxin fusion protein
INVENTOR(S): Klimpel, Kurt; Goletz, Theresa J.; Arora, Naveen; Leppla, Stephen H.; Berzofsky, Jay A.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Klimpel, Kurt; Goletz, Theresa J.; Arora, Naveen; Leppla, Stephen H.; Berzofsky, Jay A.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811914	A1	19980326	WO 1997-US16452	19970916
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743521	A1	19980414	AU 1997-43521	19970916
AU 727015	B2	20001130		
EP 957934	A1	19991124	EP 1997-941660	19970916
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-25270 P 19960917
WO 1997-US16452 W 19970916

AB The present invention provides a **vaccine** for inducing an immune response in mammal to a specific antigen, where the **vaccine** comprises a unit dose of a binary toxin **protective antigen** and the antigen, which is bound to a binary toxin **protective antigen** binding protein. In one embodiment the **vaccine** is comprised of an anthrax **protective antigen** and the antigen bound to anthrax **protective antigen** binding protein. The present invention also provides a method of **immunizing** a mammal against an antigen using the **vaccine**, and a method of inducing antigen-presenting mammalian cells to present specific antigens via the MHC class I processing pathway.

L13 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:162853 HCAPLUS

DOCUMENT NUMBER: 128:269329
TITLE: Fermentation, purification, and characterization of **protective antigen** from a recombinant, avirulent strain of Bacillus anthracis
AUTHOR(S): Farchaus, J. W.; Ribot, W. J.; Jendrek, S.; Little, S. F.
CORPORATE SOURCE: Bacteriology Division, U.S. Army Medical Research Institute of Infectious Diseases, Frederick, MD, 21702-5011, USA
SOURCE: Appl. Environ. Microbiol. (1998), 64(3), 982-991
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacillus **anthracis**, the etiol. agent for **anthrax**, produces two bipartite, AB-type exotoxins, edema toxin and **lethal** toxin. The B subunit of both exotoxins is an Mr 83,000 protein termed **protective antigen** (PA). The human **anthrax vaccine** currently licensed for use in the United States consists primarily of this protein adsorbed onto aluminum oxyhydroxide. This report describes the prodn. of PA from a recombinant, asporogenic, nontoxigenic, and nonencapsulated host strain of B. **anthracis** and the subsequent purifn. and characterization of the protein product. Fermn. in a high-tryptone, high-yeast-ext. medium under nonlimiting aeration produced 20 to 30 mg of secreted PA per L. Secreted protease activity under these fermn. conditions was low and was inhibited more than 95% by the addn. of EDTA. A purity of 88 to 93% was achieved for PA by diafiltration and anion-exchange chromatog., while greater than 95% final purity was achieved with an addnl. hydrophobic interaction chromatog. step. The purity of the PA product was characterized by reversed-phase HPLC, SDS-capillary electrophoresis, capillary isoelec. focusing, native gel electrophoresis, and SDS-PAGE. The biol. activity of the PA, when combined with excess **lethal factor** in the macrophage cell lysis assay, was comparable to previously reported values.

L13 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:773519 HCAPLUS
DOCUMENT NUMBER: 128:60505
TITLE: Passive protection by polyclonal antibodies against Bacillus anthracis infection in guinea pigs
AUTHOR(S): Little, S. F.; Ivins, B. E.; Fellows, P. F.; Friedlander, A. M.
CORPORATE SOURCE: Bacteriology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, 21702-5011, USA
SOURCE: Infect. Immun. (1997), 65(12), 5171-5175
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The protective effects of polyclonal antisera produced by injecting guinea pigs with **protective antigen** (PA), the chem. **anthrax vaccine** AVA, or Sterne spore **vaccine**, as well as those of toxin-neutralizing monoclonal antibodies (MAbs) produced against PA, **lethal factor**, and edema **factor**, were examd. in animals infected with Bacillus **anthracis** spores. Only the anti-PA polyclonal serum significantly protected the guinea pigs from death, with 67% of infected animals surviving. Although none of the MAbs was protective, one PA MAb caused a

significant delay in time to death. Our findings demonstrate that antibodies produced against only PA can provide passive protection against **anthrax** infection in guinea pigs.

L13 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:710540 HCAPLUS
DOCUMENT NUMBER: 128:12448
TITLE: Targeting HIV proteins to the major histocompatibility complex class I processing pathway with a novel gp120-anthrax toxin fusion protein
AUTHOR(S): Goletz, Theresa J.; Klimpel, Kurt R.; Arora, Naveen; Leppla, Stephen H.; Keith, Jerry M.; Berzofsky, Jay A.
CORPORATE SOURCE: Molecular Immunogenetics and Vaccine Research Section, Division of Clinical Sciences, Metabolism Branch, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1997), 94(22), 12059-12064
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A challenge for subunit **vaccines** whose goal is to elicit CD8+ cytotoxic T lymphocytes (CTLs) is to deliver the antigen to the cytosol of the living cell, where it can be processed for presentation by major histocompatibility complex (MHC) class I mols. Several bacterial toxins have evolved to efficiently deliver catalytic protein moieties to the cytosol of eukaryotic cells. **Anthrax lethal** toxin consists of two distinct proteins that combine to form the active toxin. **Protective antigen** (PA) binds to cells and is instrumental in delivering **lethal factor** (LF) to the cell cytosol. To test whether the **lethal factor** protein could be exploited for delivery of exogenous proteins to the MHC class I processing pathway, they authors constructed a genetic fusion between the amino-terminal 254 amino acid of LF and the gp120 portion of the HIV-1 envelope protein. Cells treated with this fusion protein (LF254-gp120) in the presence of PA effectively processed gp120 and presented an epitope recognized by HIV-1 gp120 V3-specific CTL. In contrast, when cells were treated with the LF254-gp120 fusion protein and a mutant PA protein defective for translocation, the cells were not able to present the epitope and were not lysed by the specific CTL. The entry into the cytosol and dependence on the classical cytosolic MHC class I pathway were confirmed by showing that antigen presentation by PA + LF254-gp120 was blocked by the proteasome inhibitor lactacystin. These data demonstrate the ability of the LF amino-terminal fragment to deliver antigens to the MHC class I pathway and provide the basis for the development of novel T cell **vaccines**.

L13 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:582554 HCAPLUS
DOCUMENT NUMBER: 125:284511
TITLE: Thermostabilization of **protective antigen**-the binding component of anthrax lethal toxin
AUTHOR(S): Radha, C.; Salotra, Poonam; Bhat, Rajiv; Bhatnagar, Rakesh
CORPORATE SOURCE: Centre for Biotechnology, Jawaharlal Nehru University, New Delhi, 110067, India
SOURCE: J. Biotechnol. (1996), 50(2,3), 235-242
CODEN: JBITD4; ISSN: 0168-1656

DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Protective antigen** (PA) is the binding component of **anthrax lethal** toxin produced by Bacillus **anthracis**, and constitutes a major ingredient of the **vaccine** against **anthrax**. PA and **lethal factor** when added together are cytolytic to mouse macrophages and J774G8 macrophage cell line. This in vitro **lethal** toxicity assay is very useful in understanding the mol. mechanism of action of **lethal** toxin. Effective utilization of PA is, however, hampered due to its thermolability. On prolonged storage at 37.degree., PA was found to lose its activity almost completely. The effect of solvent additives like trehalose, sorbitol, xylitol, sodium citrate and magnesium sulfate on the thermal stabilization of PA was examd. The results indicated an increase in the stability of PA when the incubation at 37.degree. was carried out in the presence of solvent additives used in the 1-3 M range. Magnesium sulfate helped retain the activity up to 82.7% against the control in which no additive was used, as judged by cytolytic assay using J774G8 macrophage cell line. Trehalose or sodium citrate also showed an appreciable protection of PA activity, while sorbitol or xylitol were not very effective. Competitive binding assay using radiolabeled PA showed that PA had lost capacity of binding to macrophage cells on prolonged incubation at 37.degree.. CD results at 4, 18 and 37.degree. indicated an increase in secondary structure at 37.degree. relative to that at 4 or 18.degree., supporting the activity data.

L13 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:104993 HCAPLUS
DOCUMENT NUMBER: 124:196250
TITLE: Expression and purification of anthrax toxin **protective antigen** from Escherichia coli
AUTHOR(S): Sharma, Manju; Swain, Prabodha K.; Chopra, Arun P.; Chaudhary, Vijay K.; Singh, Yogendra
CORPORATE SOURCE: Genetic Eng. Div., Centre Biochem. Technol., Delhi, 110 007, India
SOURCE: Protein Expression Purif. (1996), 7(1), 33-8
CODEN: PEXPEJ; ISSN: 1046-5928
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Anthrax** toxin consists of three sep. proteins, **protective antigen** (PA), **lethal factor** (LF), and edema **factor** (EF). PA binds to the receptor on mammalian cells and facilitates translocation of EF or LF into the cytosol. PA is the primary component of several **anthrax vaccines**. In this study the authors expressed and purified PA from Escherichia coli. The purifn. of PA from E. coli was possible after transporting the protein into the periplasmic space using the outer membrane protein A signal sequence. The purifn. involved sequential chromatog. through hydroxyapatite, DEAE Sepharose CL-4B, followed by Sephadex G-100. The typical yield of purified PA from this procedure was 500 .mu.g/L. PA expressed and purified from E. coli was similar to the PA purified from Bacillus **anthracis** in its ability to lyse a macrophage cell line (J774A.1). The present results suggest that a signal sequence is required for the efficient translocation of PA into E. coli periplasmic space.

L13 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:467447 HCAPLUS

DOCUMENT NUMBER: 122:211640
TITLE: Protective immunity induced by Bacillus anthracis toxin-deficient strains
AUTHOR(S): Pezard, Corinne; Weber, Martine; Sirard, Jean-Claude; Berche, Patrick; Mock, Michele
CORPORATE SOURCE: Lab. Genet. Mol. Toxines, Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Infect. Immun. (1995), 63(4), 1369-72
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The two toxins secreted by Bacillus **anthracis** are composed of binary combinations of three proteins: **protective antigen** (PA), **lethal factor** (LF), and edema **factor** (EF). Six mutant strains that are deficient in the prodn. of one or two of these toxin components have been previously constructed and characterized. In this work, the authors examd. the antibody response to the in vivo prodn. of PA, LF, and EF in mice **immunized** with spores of strains producing these proteins. High titers of antibody to PA were obsd. after **immunization** with all strains producing PA, while titers of antibodies to EF and LF were weak in animals **immunized** with strains producing only EF or LF. In contrast, **immunization** with strains producing either PA and EF or PA and LF resulted in an increased antibody response to EF or LF, resp. The differing levels of protection from a **lethal anthrax** challenge afforded to mice **immunized** with spores of the mutant strains not only confirm the role of PA as the major **protective antigen** in the humoral response but also indicate a significant contribution of LF and EF to immunoprotection. The authors obsd., however, that PA-deficient strains were also able to provide some protection, thereby suggesting that immune mechanisms other than the humoral response may be involved in immunity to **anthrax**. Finally, a control strain lacking the toxin-encoding plasmid was unable to provide protection or elicit an antibody response against bacterial antigens, indicating a possible role for pXO1 in the survival of B. **anthracis** in a host.

L13 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:648365 HCAPLUS
DOCUMENT NUMBER: 121:248365
TITLE: The chymotrypsin-sensitive site, FFD315, in **anthrax** toxin **protective antigen** is required for translocation of **lethal factor**
AUTHOR(S): Singh, Yogendra; Klimpel, Kurt R.; Arora, Naveen; Sharma, Manju; Leppla, Stephen H.
CORPORATE SOURCE: Cent. Biochem. Technology, Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (1994), 269(46), 29039-46
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **protective antigen** (PA) component of **anthrax** toxin contains two sites that are uniquely sensitive to proteolytic cleavage. Cleavage at the sequence RKKK167 by the cellular protease furin is absolutely required for toxicity, whereas cleavage by chymotrypsin or thermolysin at the sequence FFD315 inactivates the protein, apparently by blocking the ability of PA to translocate the catalytic moieties of the toxins, **lethal factor** (LF)

and edema **factor** (EF), to the cytosol of eukaryotic cells. To specify the role of the chymotrypsin-sensitive site of PA in the translocation of LF1 we altered resides 313-315. None of the mutations in this region interfered with the ability of PA to bind to its cellular receptor, be cleaved by cell surface furin, and bind LF. Substitution of Ala for Asp315 or for both Phe313 and Phe314 reduced the ability of PA to intoxicate cells in the presence of LF by 3- and 7-fold, resp. Substitution of Phe313 by Cys greatly reduced the rate of LF translocation and delayed toxicity. The rate at which the Cys-substituted PA killed cells was increased significantly by blocking the sulfhydryl group with iodoacetamide, suggesting that this added Cys interacts with cellular proteins and slows translocation of LF. Deletion of the 2 Phes rendered PA completely non-toxic. This deleted PA protein lacked the ability shown by native PA to form oligomers on cells and in soln. and to induce release of 86Rb from Chinese hamster ovary cells. These results suggest that the chymotrypsin-sensitive site in PA is required for membrane channel formation and translocation of LF into the cytosol. PA double mutants were constructed that cannot be cleaved at either the furin or chymotrypsin sites. These PA proteins were more stable in Bacillus **anthracis** culture supernatants and may therefore by useful as a replacement for PA in **anthrax vaccines**.

L13 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:35771 HCAPLUS
DOCUMENT NUMBER: 118:35771
TITLE: Bacillus anthracis with deletions of genes involved in toxin synthesis for use in **vaccines**
INVENTOR(S): Mock, Michele; Cataldi, Angel; Pezard, Corinne
PATENT ASSIGNEE(S): Institut Pasteur, Fr.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9219720	A1	19921112	WO 1992-FR397	19920430
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
FR 2676068	A1	19921106	FR 1991-5417	19910502
FR 2676068	B1	19941104		
EP 537342	A1	19930421	EP 1992-917387	19920430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
US 5840312	A	19981124	US 1994-325647	19941019
PRIORITY APPLN. INFO.:			FR 1991-5417	19910502
			WO 1992-FR397	19920430
			US 1993-961914	19930302

AB Genes of the plasmid pXO1 of Bacillus anthracis that play a role in the pathogenesis of anthrax are inactivated to minimize pathogenicity to allow the use of strains carrying the plasmid to be used in live **vaccines** against anthrax. The genes pag, cya, and lef of pXO1 were inactivated by insertion or deletion by std. methods. Mice infected with B. anthracis carrying these modified plasmids showed increased LD50 with the greatest effect shown when the lef gene was deleted (complete loss of virulence). Mice inoculated with B. anthracis with deletions of the cya and lef genes or the lef gene showed 90% and 85% survival upon challenge with a lethal inoculum of B. anthracis.

L13 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:192239 HCAPLUS
DOCUMENT NUMBER: 116:192239
TITLE: Serum protease cleavage of Bacillus anthracis **protective antigen**
AUTHOR(S): Ezzell, John W., Jr.; Abshire, Teresa G.
CORPORATE SOURCE: Bacteriol. Div., U. S. Army Med. Res. Inst. Infect. Dis. Fort Detrick, Frederick, MD, 21702-5011, USA
SOURCE: J. Gen. Microbiol. (1992), 138(3), 543-9
CODEN: JGMIAN; ISSN: 0022-1287
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **protective antigen** component of **anthrax** **lethal** toxin, produced in vitro, has a mol. mass of 83 kDa. Other cell culture studies have demonstrated that upon binding of the 83 kDa **protective antigen** to cell-surface receptors, the protein is cleaved by an unidentified cell-assocd. protease activity. The resultant 63 kDa protein then binds **lethal factor** to form **lethal** toxin, which has been proposed to be internalized by endocytosis. It was found that, in the blood of infected animals, the **protective antigen** exists primarily as a 63 kDa protein and appears to be complexed with the **lethal factor** component of the toxin. Conversion of **protective** **antigen** from 83 to 63 kDa was catalyzed by a calcium-dependent, heat-labile serum protease. Except for being complexed to **protective antigen**, there was no apparent alteration of **lethal factor** during the course of **anthrax** infection. The **protective antigen**-cleaving protease appeared to be ubiquitous among a wide range of animal species, including primates, horses, goats, sheep, dogs, cats and rodents.

L13 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:589232 HCAPLUS
DOCUMENT NUMBER: 111:189232
TITLE: A deleted variant of Bacillus anthracis **protective antigen** is non-toxic and blocks anthrax toxin action in vivo
AUTHOR(S): Singh, Yogendra; Chaudhary, Vijay K.; Leppla, Stephen H.
CORPORATE SOURCE: Bacteriol. Div., United States Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21701-5011, USA
SOURCE: J. Biol. Chem. (1989), 264(32), 19103-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Anthrax** toxin is the only protein secreted by B. **anthracis** that contributes to the virulence of this bacterium. An obligatory step in the action of **anthrax** toxin on eukaryotic cells is cleavage of the receptor-bound **protective** **antigen** (PA) protein (83 kilodaltons) to produce a 63-kilodalton, receptor-bound COOH-terminal fragment. A similar fragment can be obtained by limited treatment with trypsin. This proteolytic processing event exposes a site with high affinity for the other two **anthrax** toxin proteins, **lethal factor** and edema **factor** . Terminal sequencing of the purified fragment showed that the activating cleavage occurred in the sequence Arg164-Lys165-Lys166-Arg167. The gene encoding PA was mutated to delete residues 163-168, and the deleted PA was purified from a B. subtilis host. The deleted PA was not cleaved by

either trypsin or the cell-surface protease, and was non-toxic when administered with **lethal factor**. Purified, deleted PA-protected rats when administered 90 min before injection of 20 min. LDs of toxin. This mutant PA may be useful as a replacement for the PA that is the major active ingredient in the current human **anthrax vaccine**, because deleted PA is expected to have normal immunogenicity, but would not combine with trace amts. of LF and EF to cause toxicity.

L13 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:37500 HCAPLUS
DOCUMENT NUMBER: 110:37500
TITLE: Immunological analysis of cell-associated antigens of Bacillus anthracis
AUTHOR(S): Ezzell, J. W.; Abshire, T. G.
CORPORATE SOURCE: Bacteriol. Div., Army Med. Res. Inst. Infect. Dis., Fort Detrick, MD, USA
SOURCE: Report (1986), Order Nno. AD-A189584, 67 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1988, 88(12), Abstr. No. 831,228
DOCUMENT TYPE: Report
LANGUAGE: English
AB By using electrophoretic immuno-transblots, EITB (Western blots), sera from Hartley guinea pigs **vaccinated** with a veterinary live-spore **anthrax vaccine** were compared to those **vaccinated** with the human **anthrax vaccine**, consisting of aluminum hydroxide-absorbed culture proteins of B. **anthracis** strain V770-NP-1R. Sera from animals **vaccinated** with the spore **vaccine** recognized two major B. **anthracis** vegetative-cell-assocd. proteins not recognized by sera from animals receiving the human **vaccine**. These proteins, termed extractable antigens 1 (EA1) and 2 (EA2), have mol. masses of 91 and 62 kilodaltons, resp. The EA1 protein appeared to be coded by chromosomal DNA, whereas the EA2 protein was only detected in strains possessing the pX01 toxin plasmid. Both of the EA proteins were serol. distinct from the three **anthrax** toxin components, as detd. by monoclonal antibody to **protective antigen** edema **factor**, and **lethal factor**, and specific antisera to the EA proteins.

L13 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:114578 HCAPLUS
DOCUMENT NUMBER: 106:114578
TITLE: Cloning and expression of the Bacillus anthracis **protective antigen** gene in Bacillus subtillis
AUTHOR(S): Ivins, Bruce E.; Welkos, Susan L.
CORPORATE SOURCE: Bacteriol. Div., Army Med. Res. Inst. Infect. Dis., Fort Detrick, MD, USA
SOURCE: Report (1986), Order No. AD-A167995/0/GAR, 35 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1986, 86(18), Abstr. No. 640,225
DOCUMENT TYPE: Report
LANGUAGE: English
AB The gene encoding the **protective antigen** (PA) moiety of the tripartite exotoxin of B. **anthracis**, was cloned from the recombinant plasmid pSE36 into B. subtilis 1S53 by using the plasmid vector pUB110. Two clones, designated PA1 and PA2, were identified which

produced PA in liq. culture at levels of 20.5-41.9 mg/mL. This PA was identical to B. **anthracis** Sterne PA with respect to migration on SDS polyacrylamide gels and Western blot antigenic reactivity. Addn. of **lethal factor** or edema **factor** to PA1 and PA2 supernatants generated biol. active **anthrax lethal** toxin or edema-producing toxin, resp. The recombinant plasmid in PA1 (pPA101) was 7.8 kilobases in size, whereas the PA2 strain plasmid (pPA102) was 6.1 kilobases. Both plasmids had deletions extending into the insert sequence but not into the DNA encoding the PA protein. **Immunization** with the live recombinant strains protected guinea pigs from **lethal** challenge with virulent B. **anthracis** spores, and partially or completely protected rats from i.v. challenge with **anthrax lethal** toxin.

L13 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:624113 HCAPLUS
DOCUMENT NUMBER: 105:224113
TITLE: Cloning and expression of the Bacillus anthracis **protective antigen** gene in Bacillus subtilis
AUTHOR(S): Ivins, Bruce E.; Welkos, Susan L.
CORPORATE SOURCE: Div. Bacteriol., U. S. Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21701-5011, USA
SOURCE: Infect. Immun. (1986), 54(2), 537-42
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene encoding the **protective antigen** (PA) moiety of the tripartite exotoxin of B. **anthracis** was cloned from the recombinant plasmid pSE36 into B. subtilis 1S53 by using the plasmid vector pUB110. Two clones, PA1 and PA2, were identified which produced PA in liq. cultures at levels of 20.5-41.9 .mu.g/mL. This PA was identical to B. **anthracis** Sterne PA with respect to migration on SDS-PAGE and to Western blot antigenic reactivity. Addn. of **lethal factor** or edema **factor** to PA1 and PA2 supernatants generated biol. active **anthrax lethal** toxin or edema-producing toxin, resp. The recombinant plasma in PA1 (pPA101) was 7.8 kilobases, whereas the PA2 strain plasmid (pPA102) was 6.1 kilobases. Both plasmids had deletions extending into the insert sequence but not into the DNA encoding the PA protein. **Immunization** with the live recombinant strains protected guinea pigs from **lethal** challenge with virulent B. **anthracis** spores, and the **immunization** partially or completely protected rats from i.v. challenge with **anthrax lethal** toxin.

L13 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:223004 HCAPLUS
DOCUMENT NUMBER: 104:223004
TITLE: Development of antibodies to **protective antigen** and **lethal factor** components of **anthrax** toxin in humans and guinea pigs and their relevance to protective immunity
AUTHOR(S): Turnbull, Peter C. B.; Broster, Malcolm G.; Carman, J. Anthony; Manchee, Richard J.; Melling, Jack
CORPORATE SOURCE: Vaccine Res. Prod. Lab., Public Health Lab. Serv. Cent. Appl. Microbiol. Res., Salisbury/Wiltshire, SP4 0JG, UK
SOURCE: Infect. Immun. (1986), 52(2), 356-63
CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A competitive inhibition ELISA was developed to detect antibodies in serum to the **protective antigen** (PA) and **lethal factor** (LF) components of **anthrax** toxin. Current human **vaccination** schedules with an acellular **vaccine** induce predictable and lasting antibody titers to PA and, when present in the **vaccine**, to LF. Live spore **vaccines** administered to guinea pigs in a single dose conferred better protection than the human **vaccines**, although they elicited lower anti-PA and anti-LF titers at time of challenge with virulent Bacillus **anthracis**. Substantial anti-PA and anti-LF titers may not, therefore, indicate solid protective immunity against **anthrax** infection. The ELISA system was also shown to be capable of detecting anti-PA and anti-LF antibodies in the sera of individuals with histories of clin. **anthrax**. The advantage of ELISA over the Ouchterlony gel diffusion test and indirect microhemagglutination assay are demonstrated. There was a high correlation between ELISA and the indirect microhemagglutination assay; but ELISA was markedly superior in terms of reproducibility, reliability, specificity, speed, and simplicity in performance and stability of the bound antigen.

L13 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:588923 HCAPLUS
DOCUMENT NUMBER: 99:188923
TITLE: Cloning of the **protective antigen** gene of Bacillus anthracis
AUTHOR(S): Vodkin, Michael H.; Leppla, Stephen H.
CORPORATE SOURCE: Pathol. Div., U. S. Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21701, USA
SOURCE: Cell (Cambridge, Mass.) (1983), 34(2), 693-7
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tripartite protein toxin of B. **anthracis** consists of **protective antigen** (PA), edema **factor** (EF), and **lethal factor** (LF). As a 1st step in developing a more efficacious **anthrax vaccine**, recombinant plasmids contg. the PA gene were isolated. A library was constructed in the E. coli vector pBR322 from BamHI-generated fragments of the **anthrax** plasmid, pBA1. Two clones producing PA were identified by screening lysates with ELISA (enzyme-linked immunosorbent assay). Western blots revealed a full-size PA protein in the recombinant E. coli, and a cell elongation assay demonstrated biol. activity. Both pos. clones had a 6-kilobase DNA insert, which mapped in the BamHI site of the vector. The 2 inserts are the same, except that they lie in opposite orientations with respect to the vector. Thus, PA is encoded by the plasmid pBA1.

L13 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:66247 HCAPLUS
DOCUMENT NUMBER: 98:66247
TITLE: Evidence for plasmid-mediated toxin production in Bacillus anthracis
AUTHOR(S): Mikesell, Perry; Ivins, Bruce E.; Ristroph, Joseph D.; Dreier, Thomas M.
CORPORATE SOURCE: Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21701, USA
SOURCE: Infect. Immun. (1983), 39(1), 371-6
CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Large-mol.-wt. plasmids were isolated from virulent and avirulent strains of Bacillus **anthracis**. Each strain contained a single plasmid species unique in mol. wt. Bacterial strains were cured of their resident extrachromosomal gene pools by sequential passage of cultures at 42.5.degree.. Coincidental to the curing of plasmids was a loss of detectable **lethal** toxin and edema-producing activities and a dramatic decrease in **lethal factor** and **protective antigen** serol. activities. The involvement of these plasmids in the prodn. of toxin was firmly established by transformation of heat-passaged cells with plasmid DNA purified from the parent strain. The ability to produce parent strain levels of toxin was restored, and the plasmid DNA similar in mol. wt. to that isolated from the parent was reisolated from all transformants examd. Two addnl. strains of B. **anthracis**, designated Pasteur **vaccine** strains, were examd. for the ability to produce toxin and for the presence of plasmid DNA. Both strains were nontoxigenic and contained no detectable plasmid elements. Apparently, B. **anthracis** strains were cured of temp.-sensitive plasmids which code for toxin structural or regulatory proteins.

L13 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1966:406476 HCAPLUS
DOCUMENT NUMBER: 65:6476
ORIGINAL REFERENCE NO.: 65:1218c-e
TITLE: Immunologic studies of anthrax. IV. Evaluation of the immunogenicity of three components of anthrax toxin
AUTHOR(S): Mahlandt, B. G.; Klein, F.; Lincoln, R. E.; Haines, B. W.; Jones, W. I., Jr.; Friedman, R. H.
CORPORATE SOURCE: U.S. Army Biol. Labs., Fort Detrick, Frederick, MD
SOURCE: J. Immunol. (1966), 96(4), 727-33
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. ibid. 91, 431-7(1963). Components of **anthrax** toxin (edema **factor** (EF), **protective antigen** (PA), and **lethal factor** (LF)) were sepd. and tested singly at 3 dose levels and in factorial combination (J. Bacteriol. 89, 74-83(1965)), to det. their efficacy as immunogens in a resistant host (rat) and in a susceptible host (guinea pig). The LF was highly immunogenic in rats against either toxin or spore challenge. The PA was immunogenic against spore challenge in rats and guinea pigs, but was completely ineffective against toxin challenge in rats. The EF alone were nonimmunogenic. The effects of LF and PA were additive and EF added to LF, PA, or LF-PA combination interacted significantly with LF to increase resistance in the rat, but was not additive in resistance in the guinea pig. The units of toxin/ml. of terminal blood was closely related to the no. of bacilli/ml. of blood at death. Only 17% of the prechallenge serum of guinea pigs, principally among the LF treatments, produced antigen-antibody precipitin lines on Ouchterlony plates. The rat serums were all neg. in this test. The antigen used to **immunize** man and animals should contain all the toxin components for max. efficiency. 18 references.

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=> d stat que l18
L1 49 SEA FILE=HCAPLUS ABB=ON PLU=ON "GALLOWAY D"/AU OR "GALLOWAY

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                D R"/AU OR ("GALLOWAY DARRELL R"/AU OR "GALLOWAY DARRELL R"/IN
                OR "GALLOWAY DARRELL RAY"/AU)
L3          258 SEA FILE=REGISTRY ABB=ON  PLU=ON  ANTHRACIS OR ANTHRAX
L4           19 SEA FILE=REGISTRY ABB=ON  PLU=ON  LETHAL(L)FACTOR
L5           31 SEA FILE=REGISTRY ABB=ON  PLU=ON  PROTECTIVE(W)ANTIGEN
L6         9808 SEA FILE=REGISTRY ABB=ON  PLU=ON  TOXIN OR TOXINS
L7         3869 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 OR LETHAL(L)FACTOR
L8          992 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 OR PROTECTIVE(W)ANTIGEN
L9         1650 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR ?ANTHRACIS OR ?ANTHRAX
L10         193 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9(L)L7
L11         147 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L8
L12          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (VACCIN? OR IMMUNIZ?)

L13          36 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 NOT L1
L14        1179 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)(RECOMBINA? OR ?NUCLEOTID
                ? OR GENE OR GENES)
L15          68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND L9
L16          52 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 NOT (L1 OR L13)
L17      394224 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 OR ?TOXIN?
L18          50 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND (L17 OR VACCIN? OR
                IMMUNIZ?)


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L18  ANSWER 1 OF 50  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2001:866583  HCAPLUS
TITLE:                   Anthrax: A motor protein determines
                         anthrax susceptibility
AUTHOR(S):               Hanna, Philip C.
CORPORATE SOURCE:        Michigan, Department of Microbiology and Immunology,
                         University of Michigan Medical School, Ann Arbor, USA
SOURCE:                  Curr. Biol. (2001), 11(22), R905-R906
                         CODEN: CUBLE2; ISSN: 0960-9822
PUBLISHER:               Cell Press
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   A new study has found that polymorphisms in the host gene kif1C,
     which encodes a kinesin-like motor protein, det. whether mouse macrophages
     are resistant or sensitive to anthrax lethal
     toxin.  These findings may lead the way to discovering how both
     germ and host factors might contribute to a lethal
     infection.

L18  ANSWER 2 OF 50  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2001:852248  HCAPLUS
TITLE:                   Crystal structure of the anthrax lethal
                         factor
AUTHOR(S):               Pannifer, Andrew D.; Wong, Thiang Ylan;
                         Schwarzenbacher, Robert; Renatus, Martin; Petosa,
                         Carlo; Blenkowska, Jadwiga; Lacy, D. Borden; Collier,
                         R. John; Park, Sukjoon; Leppla, Stephen H.; Hanna,
                         Philip; Liddington, Robert C.
CORPORATE SOURCE:        Biochemistry Department, University of Leicester,
                         Leicester, LE1 7RH, UK
SOURCE:                  Nature (London, U. K.) (2001), 414(6860), 229-233
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CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Lethal factor** (LF) is a protein (relative mol. mass 90,000) that is crit. in the pathogenesis of **anthrax**. It is a highly specific protease that cleaves members of the mitogen-activated protein kinase kinase (MAPKK) family near to their amino termini, leading to the inhibition of one or more signalling pathways. Here we describe the crystal structure of LF and its complex with the N terminus of MAPKK-2. LF comprises four domains: domain I binds the membrane-translocating component of **anthrax toxin**, the protective antigen (PA); domains II, III and IV together create a long deep groove that holds the 16-residue N-terminal tail of MAPKK-2 before cleavage. Domain II resembles the ADP-ribosylating **toxin** from Bacillus cereus, but the active site has been mutated and recruited to augment substrate recognition. Domain III is inserted into domain II, and seems to have arisen from a repeated duplication of a structural element of domain II. Domain IV is distantly related to the zinc metalloprotease family, and contains the catalytic center; it also resembles domain I. The structure thus reveals a protein that has evolved through a process of **gene** duplication, mutation and fusion, into an enzyme with high and unusual specificity.

L18 ANSWER 3 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:785123 HCAPLUS
DOCUMENT NUMBER: 135:314545
TITLE: **Anthrax toxin**
AUTHOR(S): Bhatnagar, Rakesh; Batra, Smriti
CORPORATE SOURCE: Centre for Biotechnology, Jawaharlal Nehru University, New Delhi, 110067, India
SOURCE: Crit. Rev. Microbiol. (2001), 27(3), 167-200
CODEN: CRVMAC; ISSN: 1040-841X
PUBLISHER: CRC Press LLC
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 194 refs. **Anthrax** is primarily a disease of herbivores caused by Gram-pos., aerobic, spore-forming Bacillus **anthracis**. Humans are accidental hosts through the food of animal origin and animal products. **Anthrax** is prevalent in most parts of the globe, and cases of **anthrax** were reported from almost every country. 3 Forms of the disease were recognized: cutaneous (through skin), gastrointestinal (through alimentary tract), and pulmonary (by inhalation of spores). The major virulence **factors** of Bacillus **anthracis** are a poly-D glutamic acid capsule and a 3-component protein **exotoxin**. The **genes** coding for the **toxin** and the enzymes responsible for capsule prodn. are carried on plasmid pXO1 and pXO2, resp. The 3 proteins of the **exotoxin** are protective antigen (PA, 83 kDa), **lethal factor** (LF, 90 kDa), and edema **factor** (EF, 89 kDa). The **toxins** follow the A-B model with PA being the B moiety and LF/EF, the alternative A moieties. LF and EF are individually nontoxic, but in combination with PA form 2 **toxins** causing different pathogenic responses in animals and cultured cells. PA + LF forms the **lethal toxin** and PA + EF forms the edema **toxin**. During the process of intoxication, PA binds to the cell surface receptor and is cleaved at the sequence RKKR (167) by cell surface proteases such as furin generating a cell-bound, C-terminal 63 kDa protein (PA63). PA63 possesses a binding site to which LF or EF bind with high affinity. The complex is

then internalized by receptor-mediated endocytosis. Acidification of the vesicle leads to insertion of PA63 into the endosomal membrane and translocation of LF/EF across the bilayer into the cytosol where they exert their toxic effects. EF has a Ca- and calmodulin-dependent adenylate cyclase activity. Recent reports indicate that LF is a protease that cleaves the amino terminus of mitogen-activated protein kinase kinases 1 and 2 (MAPKK1 and 2), and this cleavage inactivates MAPKK1 and thus inhibits the mitogen-activated protein kinase signal transduction pathway. The authors describe in detail the studies so far done on unraveling the mol. mechanisms of pathogenesis of Bacillus **anthracis**.

REFERENCE COUNT: 196
REFERENCE(S): (2) Almond, B; J Biol Chem 1994, V269, P26635 HCAPLUS
(3) Arora, N; Infect Immun 1994, V62, P4955 HCAPLUS
(4) Arora, N; J Biol Chem 1992, V267, P15542 HCAPLUS
(5) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
(6) Arora, N; Mol Cell Biochem 1997, V177, P7 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:598212 HCAPLUS
DOCUMENT NUMBER: 135:177260
TITLE: FRET-based peptide biosensors for detecting **anthrax** lethal factor protease and Bacillus **anthracis**
INVENTOR(S): Burroughs-Tencza, Sarah
PATENT ASSIGNEE(S): Cellomics, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001059149	A2	20010816	WO 2001-US4253	20010209

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-182011 P 20000211
OTHER SOURCE(S): MARPAT 135:177260

AB The present invention provides fluorescence resonance energy transfer (FRET)-based protease biosensor, and kits contg. them, for detecting the presence of the lethal factor protease from Bacillus **anthracis**, as well as methods for using the protease biosensors to detect the presence of B. **anthracis** in a test sample. The present protease biosensors and assays provide a significant improvement over previous biosensors and assays for detecting B. **anthracis** in a sample, by significantly improving both the speed and efficiency of the assays, and by detecting live, virulent strains of B. **anthracis**. Therefore, the biosensors of the present invention will have fewer false positives, which is desirable for a sensor to be used in a potentially hazardous

situation.

L18 ANSWER 5 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:531617 HCAPLUS
DOCUMENT NUMBER: 135:287553
TITLE: Enhanced Expression of the **Recombinant Lethal Factor** of Bacillus **anthracis** by Fed-Batch Culture
AUTHOR(S): Gupta, Pankaj; Sahai, Vikram; Bhatnagar, Rakesh
CORPORATE SOURCE: Centre for Biotechnology, Jawaharlal Nehru University, New Delhi, 110067, India
SOURCE: Biochem. Biophys. Res. Commun. (2001), 285(4), 1025-1033
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB High cell d. cultivation has been one of the most effective ways to increase cell as well as the product yields. The structural **gene** for the 90-kDa **lethal factor** (LF) isolated from Bacillus **anthracis** was expressed as fusion protein with 6.times. histidine residues under the transcriptional regulation of the T5 promoter in Escherichia coli. Various strategies were tried to scale up the expression of the **recombinant lethal factor** by bioprocess optimization using fed batch culture technique in a 14 L fermentor. The media, a defined mixt. of salts, trace elements, vitamins, etc. along with a specified carbon source was used for the growth. The pH of the media was maintained at 6.8 while the temp. was changed from 37 to 28.degree.C during the cultivation. During the growth and induction phases, the DO was maintained above 20% by automatic control of agitation. The specific growth rate was controlled by utilizing an exponential feeding profile detd. from mass balance equations. As a result of control of specific growth rate at two different levels, there was about twenty five fold increase in biomass compared to the biomass in the shake flask. E. coli cells yielded a sol. cytosolic protein with an apparent mol. mass of 90 kDa. The protein was purified to homogeneity using metal chelate affinity chromatog., followed by anion exchange on FPLC using Mono-Q column. In soln., trypsin cleaved protective antigen bound to native and **recombinant** LF with comparable affinity. The **recombinant** LF resembled the LF purified from B. **anthracis** in the macrophage lysis assay, using a murine macrophage cell line J774A.1 sensitive to **anthrax toxin**. It was possible to achieve a yield of 50 mg of the purified protein from 1 L culture broth. (c) 2001 Academic Press.
REFERENCE COUNT: 33
REFERENCE(S): (1) Bhatnagar, R; Cell Signal 1999, V11, P111 HCAPLUS
(2) Bhatnagar, R; Infect Immun 1989, V57, P2107 HCAPLUS
(4) Bragg, T; Gene 1989, V81, P45 HCAPLUS
(5) Duesbery, N; Science 1998, V280, P734 HCAPLUS
(6) Friedlander, A; Infect Immun 1993, V61, P245 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:411501 HCAPLUS
DOCUMENT NUMBER: 135:220887
TITLE: Targeting of tumor cells by cell surface urokinase plasminogen activator-dependent **anthrax**

toxin
AUTHOR(S): Liu, Shihui; Bugge, Thomas H.; Leppla, Stephen H.
CORPORATE SOURCE: Oral Infection and Immunity Branch, NICDR, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (2001), 276(21), 17976-17984
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Urokinase plasminogen activator receptor (uPAR) binds pro-urokinase plasminogen activator (pro-uPA) and thereby localizes it near plasminogen, causing the generation of active uPA and plasmin on the cell surface. UPAR and uPA are overexpressed in a variety of human tumors and tumor cell lines, and expression of uPAR and uPA is highly correlated to tumor invasion and metastasis. To exploit these characteristics in the design of tumor cell-selective **cytotoxins**, we constructed mutated **anthrax toxin**-protective antigen (PrAg) proteins in which the furin cleavage site is replaced by sequences cleaved specifically by uPA. These uPA-targeted PrAg proteins were activated selectively on the surface of uPAR-expressing tumor cells in the presence of pro-uPA and plasminogen. The activated PrAg proteins caused internalization of a **recombinant cytotoxin**, FP59, consisting of **anthrax toxin lethal factor** residues 1-254 fused to the ADP-ribosylation domain of Pseudomonas **exotoxin** A, thereby killing the uPAR-expressing tumor cells. The activation and cytotoxicity of these uPA-targeted PrAg proteins were strictly dependent on the integrity of the tumor cell surface-assocd. plasminogen activation system. We also constructed a mutated PrAg protein that selectively killed tissue plasminogen activator-expressing cells. These mutated PrAg proteins may be useful as new therapeutic agents for cancer treatment.

REFERENCE COUNT: 81
REFERENCE(S):
(1) Andreasen, P; Cell Mol Life Sci 2000, V57, P25 HCAPLUS
(2) Arora, N; J Biol Chem 1992, V267, P15542 HCAPLUS
(3) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
(4) Astedt, B; Nature 1976, V261, P595 HCAPLUS
(5) Baker, M; Cancer Res 1990, V50, P4676 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:288566 HCAPLUS
TITLE: Genetic, Physical, and Transcript Map of the Ltxs1 Region of Mouse Chromosome 11
AUTHOR(S): Watters, James W.; Dietrich, William F.
CORPORATE SOURCE: Howard Hughes Medical Institute, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Genomics (2001), 73(2), 223-231
CODEN: GNMCEP; ISSN: 0888-7543
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Lethal factor** (LF) is a **toxin** secreted by Bacillus **anthracis** that plays an important role in the pathogenesis of **anthrax**. Intoxication with LF results in a macrophage-specific cytolysis that is not well understood. Interestingly, inbred mouse strains exhibit dramatic differences in the susceptibility of their cultured macrophages to killing by LF, and a **gene** that

influences this phenotype, called Ltxs1, has been mapped to mouse chromosome 11. Here we report a high-resoln. genetic map that confines the Ltxs1 region to a 0.51-cM interval between D11Mit90 and D11Die37/D11Die38. We have also constructed a complete phys. map of YAC and BAC clones covering the Ltxs1 region. In conjunction with synteny homol. searching, BLAST searches of sequences obtained from the clones in the phys. map have revealed 14 known **genes** and five ESTs that reside in the crit. interval. Addnl., a region of 100 kb or more is deleted in the Ltxs1 interval of some strains. Our genetic, phys., and transcript map provides an important resource for the mol. cloning of Ltxs1. (c) 2001 Academic Press.

REFERENCE COUNT: 27

REFERENCE(S):
(1) Celada, A; J Exp Med 1984, V160, P55 HCAPLUS
(2) Deloukas, P; Science 1998, V282, P744 HCAPLUS
(3) Dietrich, W; Genetics 1992, V131, P423 HCAPLUS
(4) Dietrich, W; Nature 1996, V380, P149 HCAPLUS
(5) Dietrich, W; Published erratum appears in Nature 1996, V381(6578), P172 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 50 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:230465 HCAPLUS

DOCUMENT NUMBER: 135:40601

TITLE: Role of furin in delivery of a CTL epitope of an **anthrax toxin**-fusion protein

AUTHOR(S): Zhang, Ye; Kida, Yutaka; Kuwano, Koichi; Misumi, Yoshio; Ikehara, Yukio; Arai, Sumio

CORPORATE SOURCE: Department of Microbiology, Kurume University School of Medicine, Fukuoka, 830-0011, Japan

SOURCE: Microbiol. Immunol. (2001), 45(2), 119-125
CODEN: MIIMDV; ISSN: 0385-5600

PUBLISHER: Center for Academic Publications Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Anthrax toxin lethal factor** (LF) in combination with **anthrax toxin** protective antigen (PA) was endocytosed and translocated to the cytosol of mammalian cells. Residues 1-255 of **anthrax toxin lethal factor** (LFn) was fused to a cytotoxic T lymphocyte (CTL) epitope of an influenza virus. For processing the **toxins**, PA must be cleaved into a 63-kDa fragment (PA63) by furin, which is a subtilisin-like processing endoprotease expressed by many eukaryotic cells. To test the ability of cells treated with the LFn fusion protein plus PA to deliver the epitope, CTL assay was performed. Two types of cell lines were identified, one was able to deliver CTL epitope while the other failed to efficiently deliver the epitope. To further elucidate the differences between these cells, the role of furin in these cells was examd. Disruption of the furin **gene** reduced its ability to deliver the CTL epitope. Furin expression in cells capable of efficiently delivering CTL epitope was quant. higher than in cells unable to deliver the epitope. The results suggest that furin plays a crit. role in delivery of the CTL epitope of LFn fusion protein.

REFERENCE COUNT: 30

REFERENCE(S):
(1) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
(2) Ballard, J; Infect Immun 1998, V66, P615 HCAPLUS
(3) Ballard, J; Proc Natl Acad Sci 1996, V93, P12531 HCAPLUS
(4) Barr, P; Cell 1991, V66, P1 HCAPLUS
(5) Bosshart, H; J Cell Biol 1994, V126, P1157 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:137244 HCAPLUS
DOCUMENT NUMBER: 134:198027
TITLE: Receptor-mediated uptake of an extracellular Bcl-XL fusion protein inhibits apoptosis
INVENTOR(S): Youle, Richard J.; Liu, Xiuhuai; Collier, R. John
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; President and Fellows of Harvard College
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012661	A2	20010222	WO 2000-US22293	20000815
WO 2001012661	A3	20010920		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-149220 P 19990816

AB Apoptosis-modifying fusion polypeptides and their corresponding nucleic acid mols. are disclosed. In general, the fusion protein comprises an apoptosis-modifying fragment from the Bcl-2 protein family fused with a cell-binding, targeting domain such as one derived from a bacterial **toxin**. The apoptosis-modifying fragment permits regulation of cell viability either pos. (using an anti-death Bcl-2 family member such as Bad) or neg. (using a pro-death member of the Bcl-2 family such as Bcl-xL) targeted to specific subsets of cells in vivo. Bacterial **toxins** may comprise the receptor-binding domain and/or translocation domain of diphtheria **toxin**, or the **anthrax** lethal factor. Pharmaceutical compns. comprising these polypeptides, and the use of these polypeptides to modify apoptosis are also provided.

IT **327191-05-9P 327191-06-0P 327191-07-1P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; receptor-mediated uptake of an extracellular Bcl-XL fusion protein inhibits apoptosis)

IT **327011-64-3P 327011-65-4P 327011-67-6P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**nucleotide** sequence; receptor-mediated uptake of an extracellular Bcl-XL fusion protein inhibits apoptosis)

L18 ANSWER 10 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:20301 HCAPLUS
DOCUMENT NUMBER: 134:189306
TITLE: Cytosolic delivery and characterization of the TcdB

glucosylating domain by using a heterologous protein fusion
AUTHOR(S): Spyres, Lea M.; Qa'Dan, Maen; Meader, Amy; Tomasek, James J.; Howard, Eric W.; Ballard, Jimmy D.
CORPORATE SOURCE: The Department of Botany and Microbiology, University of Oklahoma, Norman, OK, 73019-0245, USA
SOURCE: Infect. Immun. (2001), 69(1), 599-601
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB TcdB from Clostridium difficile glucosylates small GTPases (Rho, Rac, and Cdc42) and is an important virulence **factor** in the human disease pseudomembranous colitis. In these expts., in-frame genetic fusions between the **genes** for the 255 amino-terminal residues of **anthrax toxin lethal factor** (LFn) and the TcdB1-556 coding region were constructed, expressed, and purified from Escherichia coli. LFnTcdB1-556 was enzymically active and glucosylated **recombinant** RhoA, Rac, Cdc42, and substrates from cell exts. LFnTcdB1-556 plus **anthrax toxin** protective antigen intoxicated cultured mammalian cells and caused actin reorganization and mouse lethality, all similar to those caused by wild-type TcdB.
REFERENCE COUNT: 9
REFERENCE(S): (2) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
(3) Baldacini, O; Toxicon 1992, V30, P129 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:813254 HCAPLUS
DOCUMENT NUMBER: 134:111899
TITLE: Expression, crystallization and preliminary X-ray diffraction studies of **recombinant** Bacillus **anthracis lethal factor**
AUTHOR(S): Bernardi, Lorenzo; Vitale, Gaetano; Montecucco, Cesare; Musacchio, Andrea
CORPORATE SOURCE: Centro CNR Biomembrane and Dipartimento di Scienze Biomediche, Universita di Padova, Padua, 35121, Italy
SOURCE: Acta Crystallogr., Sect. D: Biol. Crystallogr. (2000), D56(11), 1449-1451
CODEN: ABCRE6; ISSN: 0907-4449
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **lethal factor** (LF) produced by Bacillus **anthracis** is a Zn2+-dependent endopeptidase which specifically cleaves the N-terminal tail of several MAP kinase kinases (MAPKKs). The **recombinant** expression, purifn. and crystn. of LF and of an inactive mutant consisting of a single amino-acid substitution in the conserved catalytic site are reported here. Both proteins crystallize in the cubic space group I432.
REFERENCE COUNT: 16
REFERENCE(S): (1) Dhanasekaran, N; Oncogene 1998, V17, P1447 HCAPLUS
(2) Duesbery, N; Science 1998, V280, P734 HCAPLUS
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(6) Hanna, P; Proc Natl Acad Sci USA 1993, V90, P10198 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:809624 HCAPLUS
DOCUMENT NUMBER: 134:95231
TITLE: Tumor cell-selective cytotoxicity of matrix metalloproteinase-activated **anthrax toxin**
AUTHOR(S): Liu, Shihui; Netzel-Arnett, Sarah; Birkedal-Hansen, Henning; Leppla, Stephen H.
CORPORATE SOURCE: Oral Infection and Immunity Branch, National Institute of Dental and Craniofacial Research, NIH, Bethesda, MD, 20892, USA
SOURCE: Cancer Res. (2000), 60(21), 6061-6067
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Matrix metalloproteinases (MMPs) are overexpressed in a variety of tumor tissues and cell lines, and their expression is highly correlated to tumor invasion and metastasis. To exploit these characteristics in the design of tumor cell-selective **cytotoxins**, we constructed two mutated **anthrax toxin** protective antigen (PA) proteins in which the furin protease cleavage site is replaced by sequences selectively cleaved by MMPs. These MMP-targeted PA proteins were activated rapidly and selectively on the surface of MMP-overexpressing tumor cells. The activated PA proteins caused internalization of a **recombinant cytotoxin**, FP59, consisting of **anthrax toxin lethal factor** residues 1-254 fused to the ADP-ribosylation domain of Pseudomonas **exotoxin** A. The toxicity of the mutated PA proteins for MMP-overexpressing cells was blocked by hydroxamate inhibitors of MMPs, including BB94, and by a tissue inhibitor of matrix metalloproteinases (TIMP-2). The mutated PA proteins killed MMP-overexpressing tumor cells while sparing nontumorigenic normal cells when these were grown together in a coculture model, indicating that PA activation occurred on the tumor cell surface and not in the supernatant. This method of achieving cell-type specificity is conceptually distinct from, and potentially synergistic with, the more common strategy of retargeting a protein **toxin** by fusion to a growth **factor**, cytokine, or antibody.
REFERENCE COUNT: 49
REFERENCE(S): (1) Arora, N; J Biol Chem 1992, V267, P15542 HCAPLUS
(2) Arora, N; J Biol Chem 1993, V268, P3334 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:688099 HCAPLUS
DOCUMENT NUMBER: 132:45555
TITLE: **Toxins** that are activated by HIV type-1 protease through removal of a signal for degradation by the N-end-rule pathway
AUTHOR(S): Falnes, Pal O.; Welker, Reinhold; Krausslich, Hans-Georg; Olsnes, Sjur

CORPORATE SOURCE: Institute for Cancer Research, The Norwegian Radium Hospital, Oslo, 0310, Norway
SOURCE: Biochem. J. (1999), 343(1), 199-207
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diphtheria **toxin** enters the cytosol of mammalian cells where it inhibits cellular protein synthesis, leading to cell death. Recently we found that the addn. of a signal for N-end-rule-mediated protein degrdn. to diphtheria **toxin** substantially reduced its intracellular stability and toxicity. These results prompted us to construct a **toxin** contg. a degrdn. signal that is removable through the action of a viral protease. In principle, such a **toxin** would be preferentially stabilized, and thus activated, in cells expressing the viral protease in the cytosol, i.e. virus-infected cells, thereby providing a specific eradication of these cells. In the present work we describe the construction of **toxins** that contain a signal for N-end-rule-mediated degrdn. just upstream of a cleavage site for the protease from HIV type 1 (HIV-1 PR). We show that the **toxins** are cleaved by HIV-1 PR exclusively at the introduced sites, and thereby are converted from unstable to stable proteins. Furthermore, this cleavage substantially increased the ability of the **toxins** to inhibit cellular protein synthesis. However, the **toxins** were unable to selectively eradicate HIV-1-infected cells, apparently due to low cytosolic HIV-1 PR activity, since we could not detect cleavage of the **toxins** by HIV-1 PR in infected cells. Alternative strategies for the construction of **toxins** that can specifically be activated by viral proteases are discussed.

REFERENCE COUNT: 35
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:681910 HCAPLUS
DOCUMENT NUMBER: 132:45625
TITLE: Sequence and organization of pXO1, the large Bacillus **anthracis** plasmid harboring the **anthrax toxin** genes
AUTHOR(S): Okinaka, R. T.; Cloud, K.; Hampton, O.; Hoffmaster, A. R.; Hill, K. K.; Keim, P.; Koehler, T. M.; Lamke, G.; Kumano, S.; Mahillon, J.; Manter, D.; Martinez, Y.; Ricke, D.; Svensson, R.; Jackson, P. J.
CORPORATE SOURCE: Life Sciences Division, Los Alamos National Laboratory, Los Alamos, NM, 87545, USA
SOURCE: J. Bacteriol. (1999), 181(20), 6509-6515
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Bacillus **anthracis** Sterne plasmid pXO1 was sequenced by random, "shotgun" cloning. A circular sequence of 181,654 bp was generated. One hundred forty-three open reading frames (ORFs) were

predicted using GeneMark and GeneMark.hmm, comprising only 61% (110,817 bp) of the pXO1 DNA sequence. The overall guanine-plus-cytosine content of the plasmid is 32.5%. The most recognizable feature of the plasmid is a "pathogenicity island," defined by a 44.8-kb region that is bordered by inverted IS1627 elements at each end. This region contains the three **toxin** genes (cya, lef, and pagA), regulatory elements controlling the **toxin** genes, three germination response genes, and 19 addnl. ORFs. Nearly 70% of the ORFs on pXO1 do not have significant similarity to sequences available in open databases. Absent from the pXO1 sequence are homologs to genes that are typically required to drive theta replication and to maintain stability of large plasmids in Bacillus spp. Among the ORFs with a high degree of similarity to known sequences are a collection of putative transposases, resolvases, and integrases, suggesting an evolution involving lateral movement of DNA among species. Among the remaining ORFs, there are three sequences that may encode enzymes responsible for the synthesis of a polysaccharide capsule usually assocd. with serotype-specific virulent streptococci.

IT **122464-80-6 244168-47-6**, Protein (plasmid pXOI gene gerXB) **244168-48-7**, Protein (plasmid pXOI gene gerXA) **244251-71-6 252728-54-4**, Protein PXO1-07 (plasmid pXO1) **252728-83-9**, Protein PXO1-13 (plasmid pXO1) **252729-01-4**, Protein PXO1-18 (plasmid pXO1) **252729-29-6**, Protein PXO1-35 (plasmid pXO1) **252729-30-9**, Protein PXO1-36 (plasmid pXO1) **252729-41-2**, Protein PXO1-39 (plasmid pXO1) **252729-46-7**, Protein PXO1-45 (plasmid pXO1) **252729-55-8**, Protein PXO1-54 (plasmid pXO1) **252729-64-9**, Protein PXO1-59 (plasmid pXO1) **252729-89-8**, Protein PXO1-79 (plasmid pXO1) **252729-91-2**, Protein PXO1-81 (plasmid pXO1) **252730-05-5**, Protein PXO1-93 (plasmid pXO1) **252730-06-6**, Protein PXO1-94 (plasmid pXO1) **252730-07-7**, Protein PXO1-95 (plasmid pXO1) **252730-08-8**, Protein PXO1-96 (plasmid pXO1) **252730-13-5**, Protein PXO1-103 (plasmid pXO1) **252730-15-7**, Protein PXO1-107 (plasmid pXO1) **252730-20-4**, Protein PXO1-110 (plasmid pXO1) **252730-22-6**, Protein PXO1-112 (plasmid pXO1) **252730-23-7**, Protein PXO1-115 (plasmid pXO1) **252730-24-8**, Protein PXO1-116 (plasmid pXO1) **252730-26-0**, Protein PXO1-119 (plasmid pXO1) **252730-27-1**, Protein PXO1-120 (plasmid pXO1) **252730-30-6**, Protein PXO1-127 (plasmid pXO1) **252730-32-8**, Protein PXO1-129 (plasmid pXO1) **252730-35-1**, Protein PXO1-132 (plasmid pXO1) **252730-39-5**, Protein PXO1-138 (plasmid pXO1) **252730-43-1**, Protein PXO1-142 (plasmid pXO1) **252749-86-3**, Protein PXO1-121 (plasmid pXO1)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; sequence and organization of pXO1, large Bacillus **anthracis** plasmid harboring **anthrax toxin genes**)

IT **225726-82-9**, GenBank AF065404
RL: BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; sequence and organization of pXO1, large Bacillus **anthracis** plasmid harboring **anthrax toxin** genes)

REFERENCE COUNT: 68

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:653908 HCAPLUS
DOCUMENT NUMBER: 132:136134
TITLE: Antigen delivery by attenuated Bacillus **anthracis**: new prospects in veterinary **vaccines**
AUTHOR(S): Brossier, F.; Mock, M.; Sirard, J.-C.
CORPORATE SOURCE: Unite Toxines et Pathogenie Bacteriennes, Institut Pasteur, Paris, Fr.
SOURCE: J. Appl. Microbiol. (1999), 87(2), 298-302
CODEN: JAMIFK; ISSN: 1364-5072
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This report summarizes the recent investigations on the use of Bacillus **anthracis** as a live vector for delivery of antigens. **Recombinant** strains were constructed by engineering the current live Sterne **vaccine**. This **vaccine**, used to prevent **anthrax** in cattle, causes side-effects due to **anthrax** **toxin** activities. Bacteria producing a genetically detoxified **toxin factor** were devoid of **lethal** effects and were as protective as the Sterne strain against exptl. **anthrax**. Moreover, B. **anthracis** expressing a foreign antigen controlled by an in vivo inducible promoter were able to generate either antibody or cellular protective responses against heterologous diseases.
REFERENCE COUNT: 20
REFERENCE(S): (1) Bartkus, J; Infection and Immunity 1989, V57, P2295 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 16 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:653907 HCAPLUS
DOCUMENT NUMBER: 132:60337
TITLE: **Anthrax** lethal factor causes proteolytic inactivation of mitogen-activated protein kinase kinase
AUTHOR(S): Duesbery, N. S.; Woude, G. F. Vande
CORPORATE SOURCE: ABL-Basic Research Program, Division of Basic Sciences, NCI-FCRDC, Frederick, MD, 21702, USA
SOURCE: J. Appl. Microbiol. (1999), 87(2), 289-293
CODEN: JAMIFK; ISSN: 1364-5072
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A search of the National Cancer Institute's Anti-Neoplastic Drug Screen for compds. with an inhibitory profile similar to that of the mitogen-activated protein kinase kinase (MAPKK) inhibitor PD098059 yielded **anthrax lethal toxin**. **Anthrax** **lethal factor** was found to inhibit progesterone-induced

meiotic maturation of frog oocytes by preventing the phosphorylation and activation of mitogen-activated protein kinase (MAPK). Similarly, **lethal toxin** prevented the activation of MAPK in serum-stimulated, ras-transformed NIH3T3 cells. In vitro analyses using **recombinant** proteins indicated that **lethal factor** proteolytically modified the NH2-terminus of both MAPKK1 and 2, rendering them inactive and hence incapable of activating MAPK. The consequences of this inactivation upon meiosis and transformed cells are also discussed.

REFERENCE COUNT: 32

REFERENCE(S):
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(2) Dudley, D; Proceedings of the National Academy of Sciences of the USA 1995, V92, P7686 HCAPLUS
(3) Duesbery, N; Science 1998, V280, P734 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:494149 HCAPLUS
DOCUMENT NUMBER: 131:238735
TITLE: Autogenous regulation of the Bacillus **anthracis** pag operon
AUTHOR(S): Hoffmaster, Alex R.; Koehler, Theresa M.
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, The University of Texas-Houston Health Science Center Medical School, Houston, TX, 77030, USA
SOURCE: J. Bacteriol. (1999), 181(15), 4485-4492
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protective antigen (PA) is an important component of the edema and **lethal toxins** produced by Bacillus **anthracis**. PA is essential for binding the **toxins** to the target cell receptor and for facilitating translocation of the enzymic **toxin** components, edema **factor** and **lethal factor**, across the target cell membrane. The structural **gene** for PA, pagA (previously known as pag), is located on the 182-kb virulence plasmic pXO1 at a locus distinct from the edema **factor** and **lethal factor genes**. Here we show that a 300-bp **gene** located downstream of pagA cotranscribed with pagA and represses expression of the operon. We have designated this **gene** pagR (for protective antigen repressor). Two pagA mRNA transcripts were detected in cells producing PA: a short, 2.7-kb transcript corresponding to the pagA **gene**, and a longer, 4.2-kb transcript representing a bicistronic message derived from pagA and pagR. The 3' end of the short transcript mapped adjacent to an inverted repeat sequence, suggesting that the sequence can act as a transcription terminator. Attenuation of termination at this site results in transcription of pagR. A pagR mutant exhibited increased steady-state levels of pagA mRNA, indicating that pagR neg. controls expression of the operon. Autogenous control of the operon may involve atxA, a trans-acting pos. regulator of pagA. The steady-state level of atxA mRNA was also increased in the pagR mutant. The mutant phenotype was complemented by addn. of pagR in trans on a multicopy plasmid.

IT **244251-71-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; autogenous regulation of the Bacillus **anthracis** pag operon)
IT **200367-48-2**, GenBank AF031382
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; autogenous regulation of the Bacillus **anthracis** pag operon)
REFERENCE COUNT: 36
REFERENCE(S): (2) Bartkus, J; Infect Immun 1989, V57, P2295 HCAPLUS
(3) Camilli, A; J Bacteriol 1990, V172, P3738 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:380524 HCAPLUS
DOCUMENT NUMBER: 131:166160
TITLE: PlcR is a pleiotropic regulator of extracellular virulence factor gene expression in Bacillus thuringiensis
AUTHOR(S): Agaisse, Herve; Gominet, Myriam; Okstad, Ole Andreas; Kolsto, Anne-Brit; Lereclus, Didier
CORPORATE SOURCE: Unite de Biochimie Microbienne, Centre National de la Recherche Scientifique URA 1300, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Mol. Microbiol. (1999), 32(5), 1043-1053
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Members of the Bacillus cereus group (B. **anthracis**, B. cereus, B. mycoides and B. thuringiensis) are well-known pathogens of mammals (B. **anthracis** and B. cereus) and insects (B. thuringiensis). The specific diseases they cause depend on their capacity to produce specific virulence **factors**, such as the **lethal toxin** of B. **anthracis** and the Cry **toxins** of B. thuringiensis. However, these Bacillus spp. also produce a variety of proteins, such as phospholipases C, which are known to act as virulence **factors** in various pathogenic bacteria. Few **genes** encoding these virulence **factors** have been characterized in pathogenic Bacillus spp. and little is known about the regulation of their expression. The authors had previously reported that in B. thuringiensis expression of the phosphatidylinositol-specific phospholipase C **gene** is regulated by the transcriptional activator PlcR. Here the authors report the identification of several extracellular virulence **factor genes** by the virtue of their PlcR-regulated expression. These PlcR-regulated **genes** encode degradative enzymes, cell-surface proteins and **enterotoxins**. The PlcR-regulated **genes** are widely dispersed on the chromosome and therefore do not constitute a pathogenic island. Anal. of the promoter region of the PlcR-regulated **genes** revealed the presence of a highly conserved palindromic region (TATGNAN4TNCATA), which is presumably the specific recognition target for PlcR activation. The authors found that the plcR **gene** is also present in and probably restricted to

all the members of the B. cereus group. However, although the polypeptide encoded by the B. cereus plcR **gene** is functionally equiv. to the B. thuringiensis regulator, the polypeptide encoded by the B. **anthracis gene** is truncated and not active as a transcriptional activator. PlcR is the first example described of a pleiotropic regulator involved in the control of extracellular virulence **factor** expression in pathogenic Bacillus spp. These results have implications for the taxonomic relationships among members of the B. cereus group, the virulence properties of these bacteria and the safety of B. thuringiensis-based biopesticides.

REFERENCE COUNT: 40

REFERENCE(S):
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(2) Agaisse, H; Mol Microbiol 1996, V20, P633 HCAPLUS
(3) Arantes, O; Gene 1991, V108, P115 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 50 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:258813 HCAPLUS
DOCUMENT NUMBER: 131:83821
TITLE: Genetic diversity in the protective antigen gene of Bacillus **anthracis**
AUTHOR(S): Price, Lance B.; Hugh-Jones, Martin; Jackson, Paul J.; Keim, Paul
CORPORATE SOURCE: Department of Biological Science, Northern Arizona University, Flagstaff, AZ, 86011-5640, USA
SOURCE: J. Bacteriol. (1999), 181(8), 2358-2362
CODEN: JOBAAY; ISSN: 0021-9193
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bacillus **anthracis** is a gram-pos. spore-forming bacterium that causes the disease **anthrax**. The **anthrax toxin** contains three components, including the protective antigen (PA), which binds to eukaryotic cell surface receptors and mediates the transport of **toxins** into the cell. In this study, the entire 2294-**nucleotide** protective antigen **gene** (pag) was sequenced from 26 of the most diverse B. **anthracis** strains to identify potential variation in the **toxin** and to further our understanding of B. **anthracis** evolution. Five point mutations, three synonymous and two missense, were identified. These differences correspond to six different haploid types, which translate into three different amino acid sequences. The two amino acid changes were shown to be located in an area near a highly antigenic region crit. to **lethal factor** binding. Nested primers were used to amplify and sequence this same region of pag from necropsy samples taken from victims of the 1979 Sverdlovsk incident. This investigation uncovered five different alleles among the strains present in the tissues, including two not seen in the 26-sample survey. One of these two alleles included a novel missense mutation, again located just adjacent to the highly antigenic region. Phylogenetic (cladistic) anal. of the pag corresponded with previous strain grouping based on chromosomal variation, suggesting that plasmid evolution in B. **anthracis** has occurred with little or no horizontal transfer between the different strains.

REFERENCE COUNT: 12

REFERENCE(S):
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(2) Duesbery, N; Science 1998, V280, P734 HCAPLUS

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 20 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:83327 HCAPLUS
DOCUMENT NUMBER: 130:264581
TITLE: Functional analysis of the carboxy-terminal domain of Bacillus **anthracis** protective antigen
AUTHOR(S): Brossier, Fabien; Sirard, Jean-Claude; Guidi-Rontani, Chantal; Duflot, Edith; Mock, Michele
CORPORATE SOURCE: Unite Toxines et Pathogenie Bacteriennes, Institut Pasteur, Paris, 75724, Fr.
SOURCE: Infect. Immun. (1999), 67(2), 964-967
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Protective antigen (PA) is the common receptor-binding component of the 2 **anthrax toxins**. The involvement of the PA carboxy-terminal domain in the interaction of the protein with cells was investigated. A deletion resulting in removal of the entire carboxy-terminal domain of PA (PA608) or part of an exposed loop of 19 amino acids (703-722) present within this domain was introduced into the pag **gene**. PA608 did not induce the **lethal-factor** (LF)-mediated cytotoxic effect on macrophages because it did not bind to the receptor. In contrast, PA711- and PA705-harboring **lethal toxins** (9- and 16-amino-acid deletions in the loop, starting after positions 711 and 705, resp.) were 10 times less cytotoxic than wild-type PA. After cleavage by trypsin, the mutant PA proteins formed heptamers and bound LF. The capacity of PA711 and PA705 to interact with cells was 1/10 that of wild-type PA. In conclusion, truncation of the carboxy-terminal domain or deletions in the exposed loop resulted in PA that was less cytotoxic or nontoxic because the mutated proteins did not efficiently bind to the receptor.
REFERENCE COUNT: 33
REFERENCE(S): (2) Blaustein, R; Proc Natl Acad Sci USA 1989, V86, P2209 HCAPLUS
(4) Choe, S; Nature 1992, V357, P216 HCAPLUS
(5) Duesbery, N; Science 1998, V280, P734 HCAPLUS
(6) Escuyer, V; Infect Immun 1991, V59, P3381 HCAPLUS
(7) Fish, D; J Bacteriol 1968, V95, P907 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:507426 HCAPLUS
DOCUMENT NUMBER: 129:198742
TITLE: Ltx1, a mouse locus that influences the susceptibility of macrophages to cytolysis caused by intoxication with Bacillus **anthracis** lethal factor, maps to chromosome 11
AUTHOR(S): Roberts, Julia E.; Watters, James W.; Ballard, Jimmy D.; Dietrich, William F.
CORPORATE SOURCE: Howard Hughes Medical Institute, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Mol. Microbiol. (1998), 29(2), 581-591

CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **lethal factor** (LF) **toxin** that is produced by Bacillus **anthracis** plays an important role in the pathogenesis of **anthrax**. LF has mononuclear phagocyte-specific intoxicating effects that are not well understood. The authors have identified genetic differences in inbred mouse strains that det. whether their cultured macrophages are susceptible to the cytolytic effect of LF intoxication. This identification of resistant and susceptible mouse strains enabled the authors to analyze crosses between these strains and to map a single responsible **gene** (called Ltx1) to chromosome 11. Ltz1 probably influences intoxication events that occur after the delivery of LF to the cytosol, as all mouse macrophages are killed by polypeptides contg. the catalytic domain of Diphtheria **toxin** fused to the domain of LF required for cytosolic transport. Furthermore, the susceptibility phenotype is dominant to resistance, suggesting that resistance is caused by an absence of or polymorphism in a mol. that acts jointly with, or downstream of, the activity of LF. This mapping of Ltx1 is a crucial first step in its positional cloning, which will provide more information about the mechanism of LF intoxication.

L18 ANSWER 22 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:152430 HCAPLUS
DOCUMENT NUMBER: 128:255031
TITLE: Regulatory factors and control of **anthrax** **toxin** gene expression
AUTHOR(S): Dai, Zhihao
CORPORATE SOURCE: Health Science Center, Univ. of Texas, Houston, TX, USA
SOURCE: (1997) 162 pp. Avail.: UMI, Order No. DA9813065 From: Diss. Abstr. Int., B 1998, 58(10), 5250
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L18 ANSWER 23 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:67814 HCAPLUS
DOCUMENT NUMBER: 128:214312
TITLE: Expression and purification of the **recombinant** **lethal factor** of Bacillus **anthracis**
AUTHOR(S): Gupta, Pankaj; Batra, Smriti; Chopra, Arun P.; Singh, Yogendra; Bhatnagar, Rakesh
CORPORATE SOURCE: Centre for Biotechnology, Jawahar Lal Nehru University, New Delhi, 110067, India
SOURCE: Infect. Immun. (1998), 66(2), 862-865
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The structural **gene** for the 90-kDa **lethal** **factor** (LF) isolated from Bacillus **anthracis** was expressed as a fusion protein with six histidine residues in Escherichia coli. Expression of LF in E. coli under the transcriptional regulation of the T5 promoter yielded a sol. cytosolic protein with an apparent mol. mass of 90 kDa, as detd. by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. **Recombinant** LF reacted with anti-LF

antibodies. The protein was purified to homogeneity by nickel nitrilotriacetic acid affinity chromatog. and gel filtration on a Sephacryl S-200 column followed by anion exchange on a fast-performance liq. chromatograph with a Resource-Q column. The yield of purified LF from this procedure was 1.5 mg/L. In soln., trypsin cleaved protective antigen bound to native and **recombinant** LF with comparable affinities. In macrophage lysis assays, native and **recombinant** LF exhibited identical potencies. The results suggest that large amts. of biol. active LF can be purified by this procedure.

L18 ANSWER 24 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:29399 HCAPLUS
DOCUMENT NUMBER: 128:98767
TITLE: Site directed mutagenesis of histidine residues in **anthrax toxin** lethal factor binding domain reduces toxicity
AUTHOR(S): Arora, Naveen
CORPORATE SOURCE: Centre for Biochemical Technology, University of Delhi, Delhi, 110007, India
SOURCE: Mol. Cell. Biochem. (1997), 177(1&2), 7-14
CODEN: MCBIB8; ISSN: 0300-8177
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Anthrax lethal toxin** is a mixt. of protective antigen (PA, 735 AA) and **lethal factor** (LF, 776 AA). Earlier studies have shown that 254 residues of **lethal factor** are sufficient for PA binding to cause internalization (Arora, N. and Leppla S. H., 1993). The present study was undertaken to det. residues which are important for binding of LF to PA. LF modification with di-Et pyrocarbonate (DEPC, modifies histidine residue primarily) results in the loss of binding and toxicity in mammalian cells. There are nine histidine residues in the binding domain. To locate the important residue(s), site-directed mutagenesis of these histidines were performed by **recombinant** methods. Replacement of His42 with Gly42 destabilizes the protein and hence it could not be purified. His35 when mutagenized to Gly35 (mLF-DTA) diminishes the toxicity by 20 fold. Time dependent studies show that binding of mLF-DTA was reduced at shorter incubations and longer incubations taper off this difference. Gel shift assay suggested 8-10% less binding of mLF-DTA as compared to LF-DTA. In conclusion His35 is important for binding and His42 is crit. and confers proper conformation for LF binding to PA.

L18 ANSWER 25 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:809419 HCAPLUS
DOCUMENT NUMBER: 128:73976
TITLE: **Anthrax** pathogenesis and host response
AUTHOR(S): Hanna, P.
CORPORATE SOURCE: Department of Microbiology, Department of Immunology, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Curr. Top. Microbiol. Immunol. (1998), 225(Bacterial Infection: Close Encounters at the Host Pathogen Interface), 13-35
CODEN: CTMIA3; ISSN: 0070-217X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 105 refs. Topics discussed include virulence plasmids and coordinate **gene** expression; **anthrax toxin**

complex; edema **factor** and **lethal factor**;
entry of **anthrax toxin** into host cells;
anthrax toxin binding to receptors; protective antigen
activation; protective antigen oligomerization; internalization;
macrophages responses to exposure to **anthrax toxin**;
and tumor necrosis **factor**-.alpha. and interleukin-1.beta..

L18 ANSWER 26 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:693600 HCAPLUS
DOCUMENT NUMBER: 127:351184
TITLE: **Anthrax toxin** fusion proteins and related methods
INVENTOR(S): Leppla, Stephen H.; Klimpel, Kurt R.; Arora, Naveen; Singh, Yogendra; Nichols, Peter J.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 60 pp. Cont.-in-part of U.S. 5,591,631.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5677274	A	19971014	US 1993-82849	19930625
US 5591631	A	19970107	US 1993-21601	19930212
CA 2155514	AA	19940818	CA 1994-2155514	19940214
WO 9418332	A2	19940818	WO 1994-US1624	19940214
WO 9418332	A3	19941013		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9463922	A1	19940829	AU 1994-63922	19940214
AU 682500	B2	19971009		
EP 684997	A1	19951206	EP 1994-911385	19940214
EP 684997	B1	19980819		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 169959	E	19980915	AT 1994-911385	19940214
ES 2122257	T3	19981216	ES 1994-911385	19940214

PRIORITY APPLN. INFO.:
US 1993-21601 A2 19930212
US 1993-82849 A 19930625
WO 1994-US1624 W 19940214

AB The present invention provides a nucleic acid encoding a fusion protein comprising a **nucleotide** sequence encoding the **anthrax** protective antigen (PA) binding domain of the native **anthrax lethal factor** (LF) protein and a **nucleotide** sequence encoding an activity-inducing domain of a second protein. Also provided is a nucleic acid encoding a fusion protein comprising a **nucleotide** sequence encoding the translocation domain and LF binding domain of the native **anthrax** PA protein and a **nucleotide** sequence encoding a ligand domain which specifically binds a cellular target. Proteins encoded by the nucleic acid of the invention, vectors comprising the nucleic acids and hosts capable of expressing the protein encoded by the nucleic acids are also provided. A compn. comprising the PA binding domain of the native LF protein chem. attached to a non-LF activity inducing moiety is further provided. A method for delivering an activity to a cell is provided. The steps of the method include (a) administering to the cell a protein comprising the translocation domain and the LF binding domain of the native PA protein and a ligand domain, and (b) administering to the cell a product

comprising the PA binding domain of the native LF protein and a non-LF activity inducing moiety, whereby the product administered in step (b) is internalized into the cell and performs the activity within the cell. The invention also provides proteins including an **anthrax** protective antigen which has been mutated to replace the trypsin cleavage site with residues recognized specifically by the HIV-1 protease.

IT **121683-96-3P 159233-84-8P 159233-86-0P**
159233-87-1P 159233-89-3P 159233-92-8P
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; **anthrax toxin** fusion proteins and related methods)

IT **140074-10-8P 140797-21-3P 159233-85-9P**
159233-88-2P 159233-90-6P 159233-91-7P
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(**nucleotide** sequence; **anthrax toxin** fusion proteins and related methods)

L18 ANSWER 27 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:254270 HCAPLUS
DOCUMENT NUMBER: 126:302511
TITLE: Detection of functional domains in the molecule of protective antigen of Bacillus **anthracis** **toxin**
AUTHOR(S): Noskov, A. N.; Kravchenko, T. B.; Noskova, V. P.
CORPORATE SOURCE: GNTs Prikl. Mikrobiol., Obolensk, Russia
SOURCE: Mol. Genet., Mikrobiol. Virusol. (1996), (3), 16-20
CODEN: MGMVDU; ISSN: 0208-0613
PUBLISHER: Meditsina
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Using the limited proteolysis method, the authors established that the protective antigen (PA) mol. of B. **anthracis exotoxin** consists of 4 functionally active domains. The shielding domain occupies an area in the linear structure of the mol. PA with N-terminal up to Lys166 and plays an important role in the proteolytic activation of PA. The associative domain situated in the Arg167-Met266 region is responsible for interactions with either **lethal** or edematous **factors** in self-assembly of the toxic complexes of the **lethal** or edematous **toxin**. The stabilizing domain occupies the Gly351-Met434 area. This area promotes the formation of conformationally stable toxic complexes with the **lethal factor**, and also directly participates in the formation of the hydrophobic canal, through which the mol. of the **lethal** or edematous **factor** and, evidently, a fragment of PA mol. as well (from Arg167 to Gly314), including the associative **gene**, gets inside the target cell. The receptor domain representing the C-terminal region, starting from Leu663, interacts with the specific receptors on macrophages and thus delivers the toxic complex to the target cell.

L18 ANSWER 28 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:490603 HCAPLUS
DOCUMENT NUMBER: 125:159517
TITLE: Genetic study of capsule and **toxin** genes expression in Bacillus **anthracis**

AUTHOR(S): Uchida, Ikuo; Makino, Souichi; Leppla, Stephen H.; Terakado, Nobuyuki
CORPORATE SOURCE: National Institute Animal Health, Tsukuba, 305, Japan
SOURCE: Mol. Approaches Food Saf.: Issues Involv. Toxic Microorg., [UJNR Int. Symp.], 8th (1995), Meeting Date 1994, 395-401. Editor(s): Eklund, Mel; Richard, John L.; Mise, Katsutoshi. Alaken: Fort Collins, Colo. CODEN: 63EFAU
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 23 refs. Virulent strains of Bacillus **anthracis** carry two plasmids which encode **genes** required for the synthesis of the major virulence **factors, anthrax toxins** and the capsule. The 96.5-kb capsule plasmid contains three **genes** necessary for synthesis of the D-glutamyl polypeptide capsule, capA, capB, and capC; and a **gene** assocd. with capsule depolymn., dep. The structural **genes** for the three **toxin** proteins pag (protective antigen **gene**), cya (edema **factor gene**) and lef (**lethal factor gene**) are located on the 184-kb **toxin** plasmid. Expression of both the capsule and **toxin** are induced by CO2. The authors have cloned the trans-acting pos. regulatory **gene** (atxA), whose product stimulates **toxin** component **genes**. The atxA **gene** was located between cya and pag on the **toxin** plasmid. Deduced amino acid of atxA has sequence similarity with that of acpA which is a trans-acting **factor** for capsule expression. Transposon mutagenesis anal. suggested that addnl. regulatory **genes** other than atxA play a role in induction of **anthrax toxin gene** expression by CO2.

L18 ANSWER 29 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:736397 HCAPLUS
DOCUMENT NUMBER: 123:277882
TITLE: The atxA gene product activates transcription of the **anthrax toxin** genes and is essential for virulence
AUTHOR(S): Dai, Zhihao; Sirard, Jean-Claude; Mock, Michele; Koehler, Theresa M.
CORPORATE SOURCE: Dep. Microbiol. Mol. Genetics, Univ. Texas-Houston, Houston, TX, 77030, USA
SOURCE: Mol. Microbiol. (1995), 16(6), 1171-81 CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacillus **anthracis** plasmid pXO1 carries the structural **genes** for the three **anthrax toxin** proteins, cya (edema **factor**), lef (**lethal factor**), and pag (protective antigen). Expression of the **toxin genes** by B. **anthracis** is enhanced during growth under elevated levels of CO2. This CO2 effect is obsd. only in the presence of another pXO1 **gene**, atxA, which encodes a transactivator of **anthrax toxin** synthesis. Here the authors show that transcription of atxA does not appear to differ in cells grown in 5% CO2 compared with cells grown in air. Using a new efficient method for **gene** replacement in B. **anthracis**, the authors constructed an atxA-null mutant in which the atxA-coding sequence on pXO1 is replaced with an .OMEGA.km-2 cassette. Transcription of all three **toxin genes** is decreased in the absence of atxA. The pag **gene** possesses two apparent transcription start sites, P1 and P2; only transcripts with 5'

ends mapping to P1 are decreased in the atxA-null mutant. Deletion anal. of the pag promoter region indicates that the 111 bp region upstream of the P1 site is sufficient for atxA-mediated activation of this transcript. The cya and lef **genes** each have one apparent start site for transcription. Transcripts with 5' ends mapping to these sites are not detected in the atxA-null mutant. The atxA-null mutant is avirulent in mice. Moreover, the antibody response to all three **toxin** proteins is decreased significantly in atxA-null mutant-infected mice. These data suggest that the atxA **gene** product also regulates **toxin gene** expression during infection.

L18 ANSWER 30 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:349189 HCAPLUS
DOCUMENT NUMBER: 122:130524
TITLE: In vitro processing of **anthrax toxin** protective antigen by recombinant PC1(SPC3) and bovine intermediate lobe secretory vesicle membranes
AUTHOR(S): Friedman, Theodore C.; Gordon, Valery M.; Leppla, Stephen H.; Klimpel, Kurt R.; Birch, Nigel P.; Loh, Y. Peng
CORPORATE SOURCE: Section Cellular Neurobiology, National Institute Child Health Human Development, Bethesda, MD, 20892, USA
SOURCE: Arch. Biochem. Biophys. (1995), 316(1), 5-13
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protective antigen (PA), an 83-kDa protein produced by Bacillus **anthracis**, requires proteolytic activation at a tetrabasic site (RKKR167) before it can combine with either edema **factor** or **lethal factor** on the cell surface. The complex is then endocytosed and the target cell intoxicated. Previous work has demonstrated that furin, a ubiquitously distributed, subtilisin-like protease, can perform this cleavage. In this study, another member of the furin family, PC1 (SPC3), was tested as a putative processing enzyme for PA. **Recombinant** PC1, partially purified from the medium of stably transfected L-cells, cleaved PA to a 63-kDa fragment (PA63) and a 20-kDa fragment (PA20). Amino-terminal sequence anal. of the 63 kDa product demonstrated that cleavage occurred between Arg167 and Ser168. The pH optimum for in vitro PA cleavage was 6.0 and the enzymic activity was calcium-dependent. Medium from untransfected L-cells did not cleave PA. Site-directed mutagenesis of the tetrabasic cleavage site revealed that PC1 preferred to cleave sequences contg. basic residues at positions -1 and -4 relative to the wild-type cleavage site, demonstrating that PC1 can cleave substrates at a monobasic residue site in vitro. Substrates having basic residues at the -1 and -2 positions were cleaved with approx. twofold less efficiency than wild-type PA. Mutants of PA contg. basic residues in positions -1 and either -2 or -4 of the cleavage site were predicted to be substrates for PC1 and were more toxic to L-cells expressing PC1 than to untransfected L-cells. These results demonstrate that PA is cleaved by PC1 in vivo. Membranes from bovine intermediate lobe secretory vesicles which contain both prohormone convertases, PC1 and PC2, also cleaved PA to PA63 with a pH optimum of 5.5. Immunodepletion studies using antisera against PC1 and PC2 showed that these are the enzymes primarily responsible for the cleavage of PA in the membrane prepn. Thus, both **recombinant** PC1 and a membrane prepn. contg. endogenous PC1 can activate PA.

L18 ANSWER 31 OF 50 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:279732 HCAPLUS
DOCUMENT NUMBER: 122:153653
TITLE: Proteolytic activation of bacterial **toxins** by eukaryotic cells is performed by furin and by additional cellular proteases
AUTHOR(S): Gordon, Valery M.; Klimpel, Kurt R.; Arora, Naveen; Henderson, Marlon A.; Leppla, Stephen H.
CORPORATE SOURCE: Lab. Microbial Ecol., Natl. Inst. Dental Res., Bethesda, MD, 20892, USA
SOURCE: Infect. Immun. (1995), 63(1), 82-7
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Before intoxication can occur, **anthrax toxin** protective antigen (PA), Pseudomonas **exotoxin** A (PE), and diphtheria **toxin** (DT) must be activated by proteolytic cleavage at specific amino acid sequences. Previously, it was shown that PA and DT can be activated by furin. In Chinese hamster ovary (CHO) cells, wild-type (RKKR) and cleavage site mutants of PA, each administered with a modified form of **anthrax toxin lethal factor** (the N terminus of **lethal factor** fused to PE domain III), had the following potencies: RKKR (wild type) (concn. causing 50% cell death [EC50] = 12 ng/mL) .gtoreq. RAAR (EC50 = 18 ng/mL) > FTKR (EC50 = 24 ng/mL) > STRR (EC50 = 49 ng/mL). In vitro cleavage of PA and cleavage site mutants of PA by furin demonstrated that native PA (RKKR) and PA with the cleavage sequence RAAR are substrates for furin. To characterize eukaryotic proteases that play a role in activating bacterial **toxins**, furin-deficient CHO cells were selected after chem. mutagenesis. Furin-deficient cells were resistant to PE, whose cleavage site, RQPR, constitutes a furin recognition site and to all PA cleavage site mutants, but were sensitive to DT (EC50 = 2.9 ng/mL) and PA (EC50 = 23 ng/mL), whose resp. cleavage sites, RKKR and RVRR, contain addnl. basic residues. Furin-deficient cells that were transfected with the furin **gene** regained sensitivity to PE and PA cleavage site mutants. These studies provide evidence that furin can activate the 3 **toxins** and that 1 or more addnl. proteases contribute to the activation of DT and PA.

L18 ANSWER 32 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:708297 HCAPLUS
DOCUMENT NUMBER: 121:308297
TITLE: **Anthrax toxin** fusion proteins for use in the targetting of cytotoxic activity
INVENTOR(S): Leppla, Stephen H.; Klimpel, Kurt; Arora, Naveen; Singh, Yogendra; Nichols, Peter J.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9418332	A2	19940818	WO 1994-US1624	19940214
WO 9418332	A3	19941013		

W: AU, CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

US 5591631	A	19970107	US 1993-21601	19930212
US 5677274	A	19971014	US 1993-82849	19930625
AU 9463922	A1	19940829	AU 1994-63922	19940214
AU 682500	B2	19971009		
EP 684997	A1	19951206	EP 1994-911385	19940214
EP 684997	B1	19980819		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1993-21601 A 19930212
US 1993-82849 A 19930625
WO 1994-US1624 W 19940214

AB Chimeric **genes** for fusion proteins of **anthrax** protective antigen (PA), the binding domain of the native **anthrax lethal factor** (LF) protein and an activity inducing domain of a second protein are described for manuf. of the protein for targetted delivery of the biol. active protein domain. The second domain may be a **toxin** or an endogenous regulator of growth or function. Chimeric **genes** for fusion proteins of a translocation domain and LF binding domain of the native **anthrax** PA protein and a ligand domain that specifically binds a cellular target are also described. The **anthrax** protective antigen may be an analog in which the trypsin cleavage site is replaced with one recognized specifically by the HIV-1 proteinase. A series of **genes** for fusion proteins of LF and Pseudomonas **exotoxins** were constructed and expressed in Escherichia coli and tested for cytotoxic activity against CHO cells. All of the fusio proteins tested were cytotoxic with the relationship between activity and the domains of the LF indicated that domain III was the active domain with domain II inhibiting this activity. A sequence (amino acids 251-278) of the Pseudomonas **exotoxin** appeared to act as a stop transfer peptide. The prepn. of fusion products with single-chain antibodies is described.

IT **121683-96-3D**, Protein PA (plasmid pXO1 clone pPA26), fusion proteins contg. **159233-84-8 159233-86-0D**, fusion proteins contg. **159233-87-1 159233-89-3 159233-92-8 159233-94-0**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; **anthrax toxin** fusion proteins for use in the targetting of cytotoxic activity)

IT **140074-10-8**, GenBank M29081 **140797-21-3**, GenBank M22589 **159233-85-9 159233-88-2 159233-90-6 159233-91-7 159233-93-9**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nucleotide** sequence; **anthrax toxin** fusion proteins for use in the targetting of cytotoxic activity)

L18 ANSWER 33 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:598143 HCAPLUS
DOCUMENT NUMBER: 121:198143
TITLE: Modified **anthrax toxin** is a potential anti-viral agent
AUTHOR(S): Leppla, S. H.; Klimpel, K. R.; Arora, N.
CORPORATE SOURCE: Laboratory of Microbial Ecology, National Institute of Dental Research, Bethesda, MD, 20892, USA
SOURCE: Zentralbl. Bakteriol., Suppl. (1994), 24(Bacterial Protein Toxins), 448-9
CODEN: ZBASE2; ISSN: 0941-018X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The amino acid sequence of the protective antigen from Bacillus **anthracis** has been changed so that the cleavage, needed to allow binding of **lethal factor** and subsequent intoxication, is performed by the HIV-1 protease. Several of the modified PA proteins are cleaved by **recombinant** HIV-1 protease.

L18 ANSWER 34 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:550452 HCAPLUS
DOCUMENT NUMBER: 121:150452
TITLE: The three Bacillus **anthracis toxin** genes are coordinately regulated by bicarbonate and temperature
AUTHOR(S): Sirard, Jean-Claude; Mock, Michele; Fouet, Agnes
CORPORATE SOURCE: Lab. Genet. Moleculaire des Toxines, Inst. Pasteur, Paris, 75724, Fr.
SOURCE: J. Bacteriol. (1994), 176(16), 5188-92
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The two Bacillus **anthracis toxins** are composed of three proteins, protective antigen, **lethal factor**, and edema **factor**. The structural **genes** for these three components are located on the virulence plasmid pX01. The authors constructed transcriptional fusions between the regulatory region of each of these **genes** and lacZ. Each construct was then inserted as a single copy at the corresponding **toxin gene** locus on pX01, resulting in three isogenic strains. Two environmental **factors**, bicarbonate and temp., were found to induce .beta.-galactosidase synthesis in each **recombinant** strain. Furthermore, the transcription of the three **toxin genes** appears to be coordinately regulated.

L18 ANSWER 35 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:549863 HCAPLUS
DOCUMENT NUMBER: 121:149863
TITLE: The development and assessment of DNA and oligonucleotide probes for the specific detection of Bacillus **anthracis**
AUTHOR(S): Hutson, R. A.; Duggleby, C. J.; Lowe, J. R.; Manchee, R. J.; Turnbull, P. C. B.
CORPORATE SOURCE: Div. Biol., PHLS Cent. Appl. Microbiol. Res., Porton Down/Salisbury/Wiltshire, UK
SOURCE: J. Appl. Bacteriol. (1993), 75(5), 463-72
CODEN: JABAA4; ISSN: 0021-8847
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two DNA probes and a no. of oligonucleotide probes were designed from the virulence factor genes of Bacillus **anthracis**. These probes were tested for specificity against 52 B. **anthracis** strains and 233 Bacillus strains encompassing 23 other species. A rapid slot blot technique was used for screening the large nos. of isolates involved. All probes tested appeared to be specific for B. **anthracis** under high stringency conditions. These probes could differentiate between virulent and avirulent strains. The probes were also applied to the detection of B. **anthracis** in routine environmental and clin. samples. A non-radioactive hybridization and detection system based on digoxigenin-11-dUTP was developed.

L18 ANSWER 36 OF 50 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:155836 HCAPLUS
DOCUMENT NUMBER: 120:155836
TITLE: Regulation of the Bacillus **anthracis** protective antigen gene: CO2 and a trans-acting element activate transcription from one of two promoters
AUTHOR(S): Koehler, Theresa M.; Dai, Zhihao; Kaufman-Yarbray, Mary
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77030, USA
SOURCE: J. Bacteriol. (1994), 176(3), 586-95
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pag of Bacillus **anthracis**, located on plasmid pXO1 (185 kb), encodes protective antigen, a component of the **anthrax lethal** and edema **toxins**. Synthesis of protective antigen is enhanced during growth of the organism with elevated levels of CO2. The CO2 effect is at the level of transcription, and pXO1-encoded regulatory **factors** have been implicated in control of pag expression. The authors used a Tn917-LTV3 insertion mutant of B. **anthracis** in which the wild-type pag **gene** on pXO1 was replaced with a pag-lacZ transcriptional fusion to monitor pag promoter activity. Expression of the pag-lacZ fusion is induced five- to eightfold during growth in 5% CO2 compared with growth in air. Growth in 20% CO2 increases transcription up to 19-fold. By monitoring pag-lacZ expression in atmospheres with different O2 and CO2 concns., the authors demonstrated definitively that the CO2 effect is specific and not simply a result of increased anaerobiosis. The results of 5' end mapping of pag transcripts indicate multiple sites of transcript initiation. The authors have detd. two major apparent start sites, designated P1 and P2, located at positions -58 and -26 relative to the translation initiation codon, resp. Anal. of total RNA from late-log-phase cells shows comparable initiation from P1 and P2 in wild-type strains grown in aerobic conditions. However, initiation from P1 is increased approx. 10-fold in cultures grown with an elevated level (5%) of CO2. The authors have identified a locus on pXO1, more than 13 kb upstream from the pag **gene**, which enhances pag transcription. When added in trans, this lucus increases the level of transcripts with 5' ends mapping to P1 but has no effect on the level of transcripts with 5' ends mapping to P2. The CO2 effect on P1 is obsd. only in the presence of the activator locus.

L18 ANSWER 37 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:4193 HCAPLUS
DOCUMENT NUMBER: 120:4193
TITLE: Construction of Bacillus **anthracis** mutant strains producing a single **toxin** component
AUTHOR(S): Pezard, Corinne; Deflot, Edith; Mock, Michele
CORPORATE SOURCE: Lab. Genet. Mol. Toxines, Inst. Pasteur, Paris, 75724, Fr.
SOURCE: J. Gen. Microbiol. (1993), 139(10), 2459-63
CODEN: JGMIAN; ISSN: 0022-1287
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The 2 protein **exotoxins** secreted by B. **anthracis** are composed of 3 distinct components: protective antigen (PA), **lethal factor** (LF), and edema **factor** (EF). A genetic strategy was developed that permits selective inactivation of each of the **genes** coding for PA, EF, or LF. This strategy involved the deletion of a portion of the structural **gene** and the insertion

of an antibiotic resistance cassette. With this technique, double mutant strains of B. **anthracis** producing only 1 **toxin** component were constructed. Characterization of the mutant strains indicated that they produced the expected single **toxin** protein. Using a simple, 2-step protocol, PA, LF, and EF were purified to homogeneity from culture supernatants. These 3 mutant strains are potentially powerful tools for studying the individual effect of each **toxin** component in vitro and in vivo.

L18 ANSWER 38 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:1840 HCAPLUS
DOCUMENT NUMBER: 120:1840
TITLE: Cloning and characterization of a gene whose product is a trans-activator of **anthrax toxin** synthesis
AUTHOR(S): Uchida, Ikuo; Hornung, Jan M.; Thorne, Curtis B.; Klimpel, Kurt R.; Leppla, Stephen H.
CORPORATE SOURCE: Lab. Microbial Ecol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SOURCE: J. Bacteriol. (1993), 175(17), 5329-38
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 184-kb Bacillus **anthracis** plasmid pXO1, which is required for virulence, contains three **genes** encoding the protein components of **anthrax toxin**, cya (edema **factor gene**), lef (**lethal factor gene**), and pag (protective antigen **gene**). Expression of the three proteins is induced by bicarbonate or serum. Using a pag-lacZ transcriptional construct to measure pag promoter activity, the authors cloned in Bacillus subtilis a **gene** (atxA) whose product acts in trans to stimulate **anthrax toxin** expression. Deletion anal. located atxA on a 2.0-kb fragment between cya and pag. DNA sequencing identified one open reading frame encoding 476 amino acids with a predicted Mr of 55,673, in good agreement with the value of 53 kDa obtained by in vitro transcription-translation anal. The cloned atxA **gene** complemented previously characterized Tn917 insertion mutants UM23 tp29 and UM23 tp32 (J. M. Hornung and C. B. Thorne, 1991), which are deficient in synthesis of all three **toxin** proteins. These results demonstrate that the atxA product activates not only transcription of pag but also that of cya and lef. .beta.-Galactosidase synthesis from the pag-lacZ transcriptional fusion construct introduced into an insertion mutant (UM23 tp62) which does not require bicarbonate for **toxin** synthesis indicated that addnl. regulatory **genes** other than atxA play a role in the induction of **anthrax toxin** **gene** expression by bicarbonate.
IT **151596-89-3**, RNA formation factor (Bacillus **anthracis** plasmid pXO1 clone pIU57 gene atxA)
RL: PRP (Properties)
(amino acid sequence of)

L18 ANSWER 39 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:17725 HCAPLUS
DOCUMENT NUMBER: 118:17725
TITLE: **Anthrax toxin** protective antigen is activated by a cell surface protease with the sequence specificity and catalytic properties of furin
AUTHOR(S): Klimpel, Kurt R.; Molloy, Sean S.; Thomas, Gary; Leppla, Stephen H.

CORPORATE SOURCE: Lab. Microb. Ecol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1992), 89(21), 10277-81
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proteolytic cleavage of the protective antigen (PA) of **anthrax toxin** at residues 164-167 is necessary for toxic activity. Cleavage by a cellular protease at this sequence, Arg-Lys-Lys-Arg, normally follows binding of PA to a cell surface receptor. The authors attempted to identify this protease by detg. its sequence specificity and catalytic properties. Semirandom cassette mutagenesis was used to generate mutants with replacements of residues 164-167 by Arg, Lys, Ser, or Asn. Anal. of 19 mutant proteins suggested that **lethal factor**-dependent toxicity required the sequence Arg-Xaa-Xaa-Arg. Based on these data, three addnl. mutants were constructed with the sequences Ala-Lys-Lys-Arg, Arg-Lys-Lys-Ala, and Arg-Ala-Ala-Arg. Of these mutant proteins, Arg-Ala-Ala-Arg was toxic, confirming that the cellular protease can recognize the sequence Arg-Xaa-Xaa-Arg. The mutant contg. the sequence Ala-Lys-Lys-Arg was also toxic but required >13 times more protein to produce equiv. toxicity. This sequence specificity is similar to that of the ubiquitous subtilisin-like protease furin, which is involved in processing of precursors of certain receptors and growth **factors**. Therefore, the authors tested whether a **recombinant** sol. furin would cleave PA. This furin deriv. efficiently cleaved native PA and the Arg-Ala-Ala-Arg mutant but not the nontoxic PA mutants. In addn., previously identified inhibitors of furin blocked cleavage of receptor-bound PA. These data imply that furin is the cellular protease that activates PA, and that nearly all cell types contain at least a small amt. of furin exposed on their cell surface.

L18 ANSWER 40 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:526179 HCAPLUS
DOCUMENT NUMBER: 117:126179
TITLE: Fusions of **anthrax toxin** lethal factor to the ADP-ribosylation domain of Pseudomonas **exotoxin** A are potent **cytotoxins** which are translocated to the cytosol of mammalian cells
AUTHOR(S): Arora, Naveen; Klimpel, Kurt R.; Singh, Yogendra; Leppla, Stephen H.
CORPORATE SOURCE: Natl. Inst. Dent. Res., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (1992), 267(22), 15542-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The lethal factor (LF) and edema factor (EF) components of **anthrax toxin** are toxic to animal cells only if internalized by interaction with the protective antigen (PA) component. PA binds to a cell surface receptor and is proteolytically cleaved to expose a binding site for LF and EF. To study how LF and EF are internalized and trafficked within cells, LF was fused to the translocation and ADP-ribosylation domains (domains II and III, resp.) of Pseudomonas **exotoxin** A. LF fusion proteins contg. Pseudomonas **exotoxin** A domains II and III were less toxic than those contg. only domain III. Fusion proteins with a functional endoplasmic reticulum retention sequence, REDLK, at the carboxyl terminus of domain III were

less toxic than those with a nonfunctional sequence, LDER. The most potent fusion protein, FP33, had an EC50 = 2 pM on Chinese hamster ovary cells, exceeding that of native Pseudomonas **exotoxin** A (EC50 = 420 pM). Toxicity of all the fusion proteins required the presence of PA and was blocked by monensin. These data suggest that LF and LF fusion proteins are efficiently translocated from acidified endosomes directly to the cytosol without trafficking through other organelles, as is required for Pseudomonas **exotoxin** A. This system provides a potential vehicle for importing diverse proteins into the cytosol of mammalian cells.

L18 ANSWER 41 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:600824 HCAPLUS
DOCUMENT NUMBER: 115:200824
TITLE: Contribution of individual **toxin** components to virulence of Bacillus **anthracis**
AUTHOR(S): Pezard, Corinne; Berche, Patrick; Mock, Michele
CORPORATE SOURCE: Unite Antigenes Bact., Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Infect. Immun. (1991), 59(10), 3472-7
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three proteins, protective antigen (PA), **lethal factor** (LF), and edema **factor** (EF; a calmodulin-dependent adenylate cyclase), compose the **lethal** (PA + LF) and edema (PA + EF) **toxins** secreted by B. **anthracis**. Mutant strains, each deficient in the prodn. of one **toxin** component, were constructed, and their virulence was then studied. A kanamycin resistance cassette was inserted in each cya (encoding EF) and lef (encoding LF) **gene**, and the constructs were sep. introduced into B. **anthracis** Sterne on a mobilizable shuttle plasmid. An EF- strain and an LF- strain were then isolated after homologous **recombination** with the resident **toxin**-encoding plasmid, pXO1. Spores from these mutants and from a previously constructed PA- mutant were used to inoculate mice, and the lethality and local edema formation were monitored. LF- or PA- mutants were not **lethal** even at high inocula, whereas the EF- mutant induced **lethal** infections. This indicates that LF in combination with PA is a key virulence **factor** required for lethality. Skin edema formation was obsd. with the LF- mutant, which produces only the combination of PA and EF. However, EF- and LF- mutants were significantly less efficient at inducing, resp., lethality and edema than was the parental Sterne strain. These results suggest that the three **toxin** components might act synergistically in vivo to cause lethality and edema formation.

L18 ANSWER 42 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:600789 HCAPLUS
DOCUMENT NUMBER: 115:200789
TITLE: Functional mapping of **anthrax toxin** lethal factor by in-frame insertion mutagenesis
AUTHOR(S): Quinn, Conrad P.; Klimpel, Kurt R.; Singh, Yogendra; Leppla, Stephen H.
CORPORATE SOURCE: Lab. Microb. Ecol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (1991), 266(30), 20124-30
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Linker insertion mutagenesis was employed to create structural disruptions of the **lethal factor** (LF) protein of **anthrax toxin** to map functional domains. A dodecameric linker was inserted at 17 blunt end restriction enzyme sites throughout the **gene**. Paired MluI restriction sites within the linker allowed the inserts to be reduced from 4 to 2 amino acids. Shuttle vectors contg. the mutated **genes** were transformed into the avirulent Bacillus **anthracis** UM23C1-1 for expression and secretion of the **gene** products. Mutations at 5 sites in the central one-third of the sequence made the protein unstable, and purified protein could not be obtained. Mutated LF proteins with insertions at the other sites were purified and assessed for toxic activity in a macrophage lysis assay and for their ability to bind to the protective antigen (PA) component of **anthrax toxin**, the receptor binding moiety. Most insertions located in the NH2-terminal one-third of the LF protein eliminated both toxicity and binding to PA, while all 4 insertions in the COOH-terminal one-third of the protein eliminated toxicity without affecting binding to PA. These data support the hypothesis that the NH2-terminal domain contains the structures required for binding to PA and the COOH-terminal domain contains the putative catalytic domain of LF.

L18 ANSWER 43 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:552821 HCAPLUS
DOCUMENT NUMBER: 115:152821
TITLE: The carboxyl-terminal end of protective antigen is required for receptor binding and **anthrax toxin** activity
AUTHOR(S): Singh, Yogendra; Klimpel, Kurt R.; Quinn, Conrad P.; Chaudhary, Vijay K.; Leppla, Stephen H.
CORPORATE SOURCE: Lab. Microb. Ecol., Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SOURCE: J. Biol. Chem. (1991), 266(23), 15493-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Anthrax toxin** consists of 3 sep. proteins produced by Bacillus **anthracis**: protective antigen (PA), **lethal factor** (LF), and edema **factor** (EF). In this report the authors more closely define a region of PA involved in receptor binding. The **gene** encoding PA was mutagenized so as to delete 3, 5, 7, 12, or 14 amino acids from the carboxyl terminus of the protein, and the truncated PA variants were purified from B. subtilis or Escherichia coli. Deletion of 3, 5, or 7 amino acids reduced the binding of PA to cells and the subsequent toxicity of the PA-LF complex to J774A.1 cells and also the ability to cause EF binding to cells. Deletion of 12 or 14 amino acids completely eliminated all these activities. These results show that the carboxy terminus comprises or is part of the receptor-binding domain of PA.

L18 ANSWER 44 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:585577 HCAPLUS
DOCUMENT NUMBER: 113:185577
TITLE: Restriction map of plasmid pXO2 and characterization of the **lethal factor gene** from Bacillus **anthracis**
AUTHOR(S): Bragg, Thomas S.
CORPORATE SOURCE: Brigham Young Univ., Provo, UT, USA
SOURCE: (1989) 103 pp. Avail.: Univ. Microfilms Int., Order No. DA9013382

From: Diss. Abstr. Int. B 1990, 50(12, Pt. 1), 5470
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L18 ANSWER 45 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:585547 HCAPLUS
DOCUMENT NUMBER: 113:185547
TITLE: Construction and characterization of a protective antigen-deficient Bacillus **anthracis** strain
AUTHOR(S): Cataldi, A.; Labruyere, E.; Mock, M.
CORPORATE SOURCE: Unite Antigenes Bact., Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Mol. Microbiol. (1990), 4(7), 1111-17
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pag **gene** coding for protective antigen (PA), one of the three **toxin** components of B. **anthracis**, has been cloned into the mobilizable shuttle vector pAT187 and transferred by conjugation from Escherichia coli to B. **anthracis**. Using this strategy, an insertionally mutated pag **gene** constructed and characterized in E. coli, was introduced into B. **anthracis** Sterne strain. This transconjugant was used to select a **recombinant** clone (RP8) carrying the inactivated pag **gene** on the **toxin**-encoding plasmid, pXO1. Strain RP8 was deficient for PA while still producing the two other **toxin** components, i.e., **lethal factor** (LF) and edema **factor** (EF). In contrast to spores from the wild-type Sterne strain, spores prepd. from RP8 were totally non-**lethal** in mice. These results clearly establish the central role played by PA in B. **anthracis** pathogenicity.

L18 ANSWER 46 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:92690 HCAPLUS
DOCUMENT NUMBER: 112:92690
TITLE: **Nucleotide** sequence and analysis of the **lethal factor gene** (lef) from Bacillus **anthracis**
AUTHOR(S): Bragg, Thomas S.; Robertson, Donald L.
CORPORATE SOURCE: Dep. Chem., Brigham Young Univ., Provo, UT, 84602, USA
SOURCE: Gene (1989), 81(1), 45-54
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **nucleotide** sequence of the B. **anthracis** **lethal factor** (LF) **gene** (lef) has been detd. LF is part of the tripartite protein **exotoxin** of B. **anthracis** along with protective antigen (PA) and edema **factor** (EF). The apparent ATG start codon, which is located immediately upstream from codons which specify the first 16 amino acids (aa) of the mature secreted LF, is preceded by an AAAGGAG sequence, which is its probable ribosome-binding site. This ATG codon begins a continuous 2427-bp open reading frame which encodes the 809-aa LF-precursor protein with an Mr of 93,798. The mature secreted protein (776 aa; Mr 90,237) was preceded by a 33-aa signal peptide which has characteristics in common with leader peptides for other secreted proteins of the Bacillus species. The codon usage of the LF **gene** reflects its high (70%) A + T content. The N-terminus of LF (first 300 aa) shared extensive homol. with

the N-terminus of the **anthrax** EF protein. Since LF and EF each bind PA at the same site, these homologous regions probably represent their common PA-binding domains.

IT **125480-65-1**, Protein LF (Bacillus **anthracis** clone pLF74/pLF71) **125480-66-2**, Protein LF (Bacillus **anthracis** clone pLF74/pLF71 precursor)
RL: PRP (Properties)
(amino acid sequence of)

IT **125479-19-8**, Deoxyribonucleic acid (Bacillus **anthracis** clone pLF74/pLF71 **gene** lef)
RL: PRP (Properties); BIOL (Biological study)
(**nucleotide** sequence of)

L18 ANSWER 47 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:418130 HCAPLUS
DOCUMENT NUMBER: 109:18130
TITLE: Molecular cloning and expression of the Bacillus **anthracis** edema factor **toxin** gene: a calmodulin-dependent adenylate cyclase
AUTHOR(S): Tippetts, M. Todd; Robertson, Donald L.
CORPORATE SOURCE: Dep. Chem., Brigham Young Univ., Provo, UT, 84602, USA
SOURCE: J. Bacteriol. (1988), 170(5), 2263-6
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The B. **anthracis exotoxin** is composed of a **lethal factor**, a protective antigen, and an edema **factor** (EF). EF is a calmodulin-dependent adenylate cyclase which elevates cAMP levels within cells. The entire EF **gene** (cva) was cloned in Escherichia coli, but EF **gene** expression by its own B. **anthracis** promoter could not be detected in E. coli. However, when the EF **gene** was placed downstream from the lac or the T7 promoter, enzymically active EF was produced. The EF **gene**, like the protective antigen (pag) and **lethal factor** (lef) **genes**, was present on the large B. **anthracis toxin** plasmid pXO1.

L18 ANSWER 48 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:585237 HCAPLUS
DOCUMENT NUMBER: 105:185237
TITLE: Molecular cloning and expression in Escherichia coli of the **lethal factor gene** of Bacillus **anthracis**
AUTHOR(S): Robertson, Donald L.; Leppla, Stephen H.
CORPORATE SOURCE: Dep. Chem., Brigham Young Univ., Provo, UT, 84602, USA
SOURCE: Gene (1986), 44(1), 71-8
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **lethal factor** (LF) **gene** of B. **anthracis** was cloned and expressed in E. coli,. At least 2 of the 6 LF **recombinant** plasmids produce full-length LF protein. Transcription of the LF **gene** in E. coli appears to be under the control of its own B. **anthracis** promoter. **Recombinant** LF protein produced in E. coli remains intracellular and is not secreted. However, this LF protein is biochem. active and displays the same **lethal** effect as LF secreted by B. **anthracis** in the mouse macrophage assay. The LF **gene**, like that of the protective antigen **gene**, is present on the large B.

anthracis toxin plasmid pXO1.

L18 ANSWER 49 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:216599 HCAPLUS
DOCUMENT NUMBER: 102:216599
TITLE: **Anthrax toxin**
AUTHOR(S): Leppla, S. H.; Ivins, B. E.; Ezzell, J. W.
CORPORATE SOURCE: Army Med. Res. Inst. Infect. Dis., Fort Detrick, MD, USA
SOURCE: Report (1984), Order No. AD-A148936/8/GAR, 16 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1985, 85(7), 34
DOCUMENT TYPE: Report
LANGUAGE: English
AB **Anthrax toxin** is a key virulence **factor** of Bacillus **anthracis**. The 3 protein components of the **toxin** have been purified and shown to have similar mol. wts.: protective antigen (PA), 85,000; **lethal factor** (LF), 83,000; edema **factor** (EF), 89,000. The edema **factors** acts by reusing the cAMP in animal cells, and subsequently EF was found to be a calmodulin-dependent adenylate cyclase. The similarity of EF to Bordetella pertussis and eukaryotic cyclases suggests that the **anthrax** EF **gene** may have originated in animals. The **lethal factor** causes death in rats in as little as 38 min. No cultured cells are known which are rapidly damaged by LF.

L18 ANSWER 50 OF 50 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1971:97323 HCAPLUS
DOCUMENT NUMBER: 74:97323
TITLE: Differentiation of the toxicity on mice of Bacillus cereus and Bacillus thuringiensis from the pathogenicity of Bacillus **anthracis** on mice
AUTHOR(S): Krieg, Aloysius
CORPORATE SOURCE: Biol. Bundesanst. Land-Forstwirtsch., Inst. Biol. Schaedingsbekaempf., Darmstadt, Ger.
SOURCE: Zentralbl. Bakteriol., Parasitenk., Infektionskr. Hyg., Abt. 1: Orig. (1970), 215(4), 523-9
CODEN: ZBPHA6
DOCUMENT TYPE: Journal
LANGUAGE: German
AB In contrast to B. **anthracis**, strains of B. cereus in the logarithmic phase produced large amts. of a proteinaceous heat-sensitive **exotoxin** which was highly toxic to mice. The same **lethal factor** was produced by B. thuringiensis. Another **exotoxin** (of **nucleotide** structure) which was heat-stable and produced only by certain strains of B. thuringiensis was highly toxic for insects, but not particularly so to mice. In addn., a heat-sensitive **endotoxin** of proteinaceous character was toxic to some insects, but not mice; it is formed as parasporal crystals only by B. thuringiensis. Spores and vegetative cells of B. cereus and B. thuringiensis were avirulent for mice in contrast to spores and vegetative cells of encapsulated strains of B. **anthracis**, which were extremely virulent for mice.

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                3/BI OR 327011-67-6/BI OR 327191-06-0/BI O

=> d ide can 1-59

L20  ANSWER 1 OF 59  REGISTRY  COPYRIGHT 2001 ACS
RN   327191-07-1  REGISTRY
CN   1-233-Protein Bcl-xL (human) fusion protein with peptide (synthetic
     linker) fusion protein with 384-535-diphtheria toxin (Corynebacterium
     diphtheriae) (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   2: PN: WO0112661 SEQID: 2 claimed protein
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1967 TO DATE)
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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198027

L20 ANSWER 2 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **327191-06-0** REGISTRY
CN 1-255-Anthrax toxin protein LF (lethal factor) (Bacillus anthracis) fusion protein with 1-209-protein Bcl-xL (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7: PN: WO0112661 SEQID: 8 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198027

L20 ANSWER 3 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **327191-05-9** REGISTRY
CN Apoptosis-regulating protein Bad (human) fusion protein with 194-535-diphtheria toxin (Corynebacterium diphtheriae) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: WO0112661 SEQID: 4 claimed protein
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198027

L20 ANSWER 4 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **327011-67-6** REGISTRY
CN DNA (synthetic Bacillus anthracis 1-255-anthrax toxin protein LF (lethal factor) fusion protein with human 1-209-protein Bcl-xL-specifying) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6: PN: WO0112661 SEQID: 7 claimed DNA
CN GenBank AX085496
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198027

L20 ANSWER 5 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **327011-65-4** REGISTRY
CN DNA (synthetic human apoptosis-regulating protein Bad fusion protein with Corynebacterium diphtheriae 194-535-diphtheria toxin-specifying) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: WO0112661 SEQID: 3 claimed DNA
CN GenBank AX085492
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198027

L20 ANSWER 6 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **327011-64-3** REGISTRY
CN DNA (synthetic human 1-233-protein Bcl-xL fusion protein with synthetic linker peptide fusion protein with Corynebacterium diphtheriae 384-535-diphtheria toxin-specifying) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0112661 SEQID: 1 claimed DNA
CN GenBank AX085490
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:198027

L20 ANSWER 7 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252749-86-3** REGISTRY
CN Protein PXO1-121 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Adenine phosphoribosyl transferase PXO1-121 (Bacillus anthracis strain Sterne plasmid pXO1 gene apt)
CN GenBank AF065404-derived protein GI 4894337
FS PROTEIN SEQUENCE
MF C275 H461 N65 O87 S2
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 8 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-43-1** REGISTRY
CN Protein PXO1-142 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894357
CN Topoisomerase-1 PXO1-142 (Bacillus anthracis strain Sterne plasmid pXO1 gene topl)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 9 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-39-5** REGISTRY
CN Protein PXO1-138 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894353
CN Small DNA-binding protein PXO1-138 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 10 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-35-1** REGISTRY
CN Protein PXO1-132 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894348
CN Intergase PXO1-132 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 11 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-32-8** REGISTRY
CN Protein PXO1-129 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894345
CN Truncated transposase PXO1-129 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 12 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-30-6** REGISTRY
CN Protein PXO1-127 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894343
CN Transposase PXO1-127 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 13 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-27-1** REGISTRY
CN Protein PXO1-120 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894336
CN Transposase PXO1-120 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 14 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-26-0** REGISTRY
CN Protein PXO1-119 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894335
CN Transcription factor PXO1-119 (Bacillus anthracis strain Sterne plasmid pXO1 gene atxA)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 15 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-24-8** REGISTRY
CN Protein PXO1-116 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894332
CN Transposase PXO1-116 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 16 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-23-7** REGISTRY
CN Protein PXO1-115 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894331
CN Resolvase PXO1-115 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 17 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-22-6** REGISTRY
CN Protein PXO1-112 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894328
CN Spore germination response protein PXO1-112 (Bacillus anthracis strain Sterne plasmid pXO1 gene gerXC)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 18 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-20-4** REGISTRY
CN Protein PXO1-110 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Anthrax toxin protective antigen PXO1-110 (Bacillus anthracis strain Sterne plasmid pXO1 gene pagA)
CN GenBank AF065404-derived protein GI 4894326
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 19 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-15-7** REGISTRY
CN Protein PXO1-107 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Anthrax toxin lethal factor PXO1-107 (Bacillus anthracis strain Sterne plasmid pXO1 gene lef)
CN GenBank AF065404-derived protein GI 4894323
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 20 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-13-5** REGISTRY
CN Protein PXO1-103 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894320
CN Intergase/recombinase PXO1-103 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 21 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-08-8** REGISTRY
CN Protein PXO1-96 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894312
CN Transposase PXO1-96 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 22 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-07-7** REGISTRY
CN Protein PXO1-95 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894311
CN NDP-sugar-dehydrogenase PXO1-95 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE. ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 23 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-06-6** REGISTRY
CN Protein PXO1-94 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894310
CN UDP-glucose-pyrophosphorylase PXO1-94 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 24 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252730-05-5** REGISTRY
CN Protein PXO1-93 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894309
CN Hyaluronate synthase PXO1-93 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 25 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-91-2** REGISTRY
CN Protein PXO1-81 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894297
CN Ras- and transposon-related protein PXO1-81 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 26 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-89-8** REGISTRY
CN Protein PXO1-79 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894295
CN Hydrophobic protein PXO1-79 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 27 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-64-9** REGISTRY
CN Protein PXO1-59 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894275
CN Secretory protein kinase PXO1-59 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 28 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-55-8** REGISTRY
CN Protein PXO1-54 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894270
CN S-layer precursor/surface layer protein PXO1-54 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 29 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-46-7** REGISTRY
CN Protein PXO1-45 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Cell division protein PXO1-45 (Bacillus anthracis strain Sterne plasmid pXO1)
CN GenBank AF065404-derived protein GI 4894261
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 30 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-41-2** REGISTRY
CN Protein PXO1-39 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894255
CN Transposase PXO1-39 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 31 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-30-9** REGISTRY
CN Protein PXO1-36 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894252
CN Transposase PXO1-36 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 32 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-29-6** REGISTRY
CN Protein PXO1-35 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894251
CN Transposase PXO1-35 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 33 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252729-01-4** REGISTRY
CN Protein PXO1-18 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894234
CN Intergase/recombinase PXO1-18 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 34 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252728-83-9** REGISTRY
CN Protein PXO1-13 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Erythrocyte invasion/rhoptry protein PXO1-13 (Bacillus anthracis strain Sterne plasmid pXO1)
CN GenBank AF065404-derived protein GI 4894229
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 35 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **252728-54-4** REGISTRY
CN Protein PXO1-07 (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894223
CN Nucleotidyltransferase, deoxyribonucleate, RNA-dependent PXO1-07 (Bacillus anthracis strain Sterne plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 36 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **244251-71-6** REGISTRY
CN Protein (Bacillus anthracis strain UM44 gene pagR) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF031382-derived protein GI 2642588
CN GenBank AF065404-derived protein GI 4894325
CN Protein PXO1-109 (plasmid pXO1)
CN Small DNA-binding protein PXO1-109 (Bacillus anthracis strain Sterne plasmid pXO1 gene pagR)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

REFERENCE 2: 131:238735

L20 ANSWER 37 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **244168-48-7** REGISTRY
CN Protein (plasmid pXOI gene gerXA) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894329
CN GenBank AF108144-derived protein GI 4092084
CN Protein PXO1-113 (plasmid pXO1)

CN Spore germination protein (Bacillus anthracis strain Sterne plasmid pXOI gene gerXA)
CN Spore germination response protein PXO1-113 (Bacillus anthracis strain Sterne plasmid pXO1 gene gerXA)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

REFERENCE 2: 131:238588

L20 ANSWER 38 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **244168-47-6** REGISTRY
CN Protein (plasmid pXOI gene gerXB) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF065404-derived protein GI 4894330
CN GenBank AF108144-derived protein GI 4092083
CN Protein PXO1-114 (plasmid pXO1)
CN Spore germination protein (Bacillus anthracis strain Sterne plasmid pXOI gene gerXB)
CN Spore germination response protein PXO1-114 (Bacillus anthracis strain Sterne plasmid pXO1 gene gerXB)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

REFERENCE 2: 131:238588

L20 ANSWER 39 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **225726-82-9** REGISTRY
CN DNA (plasmid pXO1) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN DNA (Bacillus anthracis strain Sterne plasmid pXO1)
CN GenBank AF065404
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

L20 ANSWER 40 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **200367-48-2** REGISTRY
CN DNA (Bacillus anthracis strain UM44 gene pagR) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AF031382
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:238735

L20 ANSWER 41 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-94-0** REGISTRY
CN Protein PA substitution derivative (plasmid pXO1 clone pPA26 protective antigen) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Protein PA (Bacillus anthracis plasmid pXO1 clone pPA26 protective antigen substituted with HIV-1 retropepsin cleavage site)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:308297

L20 ANSWER 42 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-93-9** REGISTRY
CN DNA (plasmid pXO1 clone pPA26 protective antigen protein PA substitution derivative-specifying) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (plasmid pXO1 clone pPA26 protective antigen protein PA substitution derivative-specifying)
OTHER NAMES:
CN DNA (Bacillus anthracis plasmid pXO1 clone pPA26 protective antigen protein PA substituted with HIV-1 retropepsin cleavage site-specifying)
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:308297

L20 ANSWER 43 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-92-8** REGISTRY
CN 1-725-Protein PA (plasmid pXO1 clone pPA26 protective antigen) fusion protein with 1-178-antigen CD 4 (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-725-Protein PA (Bacillus anthracis anthrax toxin protective antigen) fusion protein with 1-178-CD4 antigen (human)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 44 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-91-7** REGISTRY
CN DNA (plasmid pXO1 clone pPA26 1-725-protective antigen protein PA fusion protein with human 1-178-CD4 (antigen)-specifying) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (plasmid pXO1 clone pPA26 1-725-protective antigen protein PA fusion protein with human 1-178-antigen CD 4-specifying)
OTHER NAMES:
CN DNA (1-725-Protein PA (Bacillus anthracis anthrax toxin protective antigen) fusion protein with 1-178-CD4 antigen (human) cDNA)
CN GenBank I33400
CN GenBank I69378
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 45 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-90-6** REGISTRY
CN DNA (Bacillus anthracis 1-254-lethal factor protein LF fusion protein with

Pseudomonas 362-613-exotoxin A-specifying) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (Bacillus anthracis 1-254-lethal factor protein LF fusion protein with Pseudomonas 362-613-exotoxin A-specifying)
OTHER NAMES:
CN DNA (1-254-Protein LF (Bacillus anthracis anthrax toxin lethal factor) fusion protein with 362-613-exotoxin A (Pseudomonas) cDNA)
CN GenBank I33399
CN GenBank I69377
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 46 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-89-3** REGISTRY
CN 1-254-Protein LF (Bacillus anthracis lethal factor) fusion protein with 362-613-exotoxin A (Pseudomonas) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-254-Protein LF (Bacillus anthracis anthrax toxin lethal factor) fusion protein with 362-613-exotoxin A (Pseudomonas)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 47 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-88-2** REGISTRY
CN DNA (Bacillus anthracis 1-254-lethal factor protein LF [methionyl-valyl-prolyl] fusion protein with Pseudomonas 398-613-exotoxin A-specifying plus 3'-flank) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (Bacillus anthracis 1-254-lethal factor protein LF [methionyl-valyl-prolyl] fusion protein with Pseudomonas 398-613-exotoxin A-specifying plus 3'-flanking region fragment)
OTHER NAMES:
CN DNA (1-254-protein LF (Bacillus anthracis anthrax toxin lethal factor) fusion protein with 398-613-exotoxin A (Pseudomonas) cDNA plus 3'-flank)
CN GenBank I33398

CN GenBank I69376
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 48 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-87-1** REGISTRY
CN 1-254-Protein LF [methionyl-valyl-prolyl] (Bacillus anthracis lethal factor) fusion protein with 398-613-exotoxin A (Pseudomonas) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-254-Protein LF (Bacillus anthracis anthrax toxin lethal factor) fusion protein with 398-613-exotoxin A (Pseudomonas)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 49 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-86-0** REGISTRY
CN Protein LF (Bacillus anthracis lethal factor) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO0145639 FIGURE: 1 claimed protein
CN Anthrax toxin lethal factor (Bacillus anthracis)
CN Protein LF (Bacillus anthracis anthrax toxin lethal factor)
CN Protein LF (lethal factor) (Bacillus anthracis)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
3 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:75730

REFERENCE 2: 127:351184

REFERENCE 3: 121:308297

L20 ANSWER 50 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-85-9** REGISTRY
CN DNA (Bacillus anthracis 1-254-lethal factor protein LF fusion protein with Pseudomonas 401-602-exotoxin A-specifying) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (Bacillus anthracis 1-254-lethal factor protein LF fusion protein with Pseudomonas 401-602-exotoxin A-specifying)
OTHER NAMES:
CN DNA (1-254-protein LF (Bacillus anthracis anthrax toxin lethal factor) fusion protein with 401-602-exotoxin A (Pseudomonas) cDNA)
CN GenBank I33397
CN GenBank I69375
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 51 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **159233-84-8** REGISTRY
CN 1-254-Protein LF (Bacillus anthracis lethal factor) fusion protein with 401-602-exotoxin A (Pseudomonas) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-254-Protein LF (Bacillus anthracis anthrax toxin lethal factor) fusion protein with 401-602-exotoxin A (Pseudomonas)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 52 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **151596-89-3** REGISTRY
CN RNA formation factor (plasmid pXO1 clone pIU57 gene atxA reduced) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Ribonucleic acid formation factor (plasmid pXO1 clone pIU57 gene atxA reduced)
OTHER NAMES:
CN RNA formation factor (Bacillus anthracis plasmid pXO1 clone pIU57 gene atxA)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:1840

L20 ANSWER 53 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **140797-21-3** REGISTRY
CN DNA (plasmid pXO1 clone pPA26 protective antigen protein PA gene plus flanks) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (plasmid pXO1 clone pPA26 protective antigen protein PA gene plus 5'- and 3'-flanking region fragment)
OTHER NAMES:
CN DNA (Bacillus anthracis plasmid pXO1 clone pPA26 anthrax toxin protective antigen gene plus flanks)
CN DNA (Bacillus anthracis protein PA (anthrax toxin protective antigen) gene plus flanks)
CN GenBank I33396
CN GenBank I69374
CN GenBank M22589
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: BIOSIS, CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 54 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **140074-10-8** REGISTRY
CN DNA (Bacillus anthracis clone pLF74 lethal factor protein LF gene plus flanks) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (Bacillus anthracis clone pLF74 lethal factor protein LF gene plus 5'- and 3'-flanking region fragment)
OTHER NAMES:
CN DNA (Bacillus anthracis protein LF (anthrax toxin lethal factor) gene plus flanks)

CN GenBank I33395
CN GenBank I69373
CN GenBank M29081
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR GenBank
LC STN Files: CA, CAPLUS, GENBANK, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:351184

REFERENCE 2: 121:308297

L20 ANSWER 55 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **125480-66-2** REGISTRY
CN Protein LF (Bacillus anthracis clone pLF74/pLF71 precursor) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:92690

L20 ANSWER 56 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **125480-65-1** REGISTRY
CN Protein LF (Bacillus anthracis clone pLF74/pLF71) (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 112:92690

L20 ANSWER 57 OF 59 REGISTRY COPYRIGHT 2001 ACS
RN **125479-19-8** REGISTRY
CN DNA (Bacillus anthracis clone pLF74/pLF71 gene lef) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Deoxyribonucleic acid (Bacillus anthracis clone pLF74/pLF71 gene lef)
OTHER NAMES:
CN 1: PN: WO0145639 FIGURE: 1 claimed DNA
CN DNA (Bacillus anthracis protein LF (lethal factor) cDNA)

FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:75730

REFERENCE 2: 112:92690

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RN **122464-80-6** REGISTRY
CN Cyclase, adenylate (Bacillus anthracis clone pMMA8812 precursor) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Calmodulin-sensitive adenylate cyclase/edema factor PXO1-122 (Bacillus anthracis strain Sterne plasmid pXO1 gene cya)
CN GenBank AF065404-derived protein GI 4894338
CN Protein PXO1-122 (plasmid pXO1)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:45625

REFERENCE 2: 113:225815

REFERENCE 3: 111:111536

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RN **121683-96-3** REGISTRY
CN Protein PA (plasmid pXO1 clone pPA26 protective antigen) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: WO0145639 FIGURE: 2 claimed protein
CN Anthrax toxin protective antigen (Bacillus anthracis plasmid pXO1 clone pPA26)
CN Antigen PA (protective antigen) (Bacillus anthracis)
CN Protein PA (Bacillus anthracis anthrax toxin protective antigen)
FS PROTEIN SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

4 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:75730

REFERENCE 2: 127:351184

REFERENCE 3: 121:308297

REFERENCE 4: 111:72002